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OBSERVATIONS ON THE USE OF *AMMI MAJUS* LINN. IN VITILIGO.

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THE crystalline extracts of *Ammi majus* Linn. have been used and proved to be of remarkable specific effect in treating leucodermia. This has been shown in two previous papers on the subject (El-Mofty, 1948, 1952), and by other workers (Sidi and Bourjeois-Gavardin, 1952; Tzanck *et al.*, 1952). Experiments with this drug showed that a high percentage of cases of vitiligo promptly responded and completely recovered or greatly improved within relatively short periods—either during or immediately after treatment. This proved the advantages of the drug as compared with all other previous lines of treatment, where failure was the rule and some improvement was the exception. The best results were obtained when all the crystalline constituents of *Ammi majus* Linn. were given orally, and the areas painted and exposed to ultraviolet rays (El-Mofty, 1952).

Local application only of the drug to leucodermic areas as a paint together with ultraviolet irradiation gave prompt response in some cases. In some of these cases certain areas were left untreated as a control, and the results obtained were convincing; the treated areas responded by pigmentation and the control areas did not change. Thus it has been proved almost beyond doubt that the drug has a direct local effect on the process of melanogenesis.

The idea of introducing the substance intradermally was conceived in order to ensure a higher concentration of the drug locally near the dormant melanoblasts in the leucodermic areas, since we lack a vehicle ensuring sufficient percutaneous penetration. It was thought that by using this new route of administration some light might be thrown on the mechanism of action of the drug on melanogenesis.

The following groups of cases have been studied using the intradermal route :

(1) Patients who had proved refractory to systemic treatment continued for a sufficient period of time. It was thought that attaining a high local concentration in the area involved might overcome this refractoriness. In patients under general treatment there is the possibility of failure of the drug to reach the area concerned in sufficient concentration.

(2) Patients who show some resistant vitiliginous areas, failing to respond to oral medication and local painting, in spite of good response and cure of extensive other areas.

(3) Patients showing only small localized lesions where it is thought advisable to avoid exposing the whole body to the action of the drug.

(4) Patients thought to be unfit for general treatment such as those with renal or liver disease, hypertension or arteriosclerosis. These patients are considered as a group in which general administration of the drug is to be avoided.

Method.—The intradermal injections were prepared in 2 c.c. ampoules, each c.c. containing 0·0625 mg. Ammoidin and 0·0375 mg. Ammidin.

Three to 40 local intradermal injections of 0·1 to 0·2 c c. of the fluid were given in one sitting once weekly. The needle was inserted at the junction of leucodermic and normal skin, and injections were worked gradually, on subsequent sittings, centripetally towards the centre of the white patch. The areas were irradiated twice weekly, once directly after the injection, and again three days later. It was done with an ordinary alpine ray lamp, at a distance of about 50 cm., and given in increasing doses to produce erythema only. Irradiation was enough to evoke erythema persisting for some time, but vesicular and bullous reactions were avoided. The treatment was continued for 2 to 7 months.

Cases receiving intradermal injections only and failing to show any reaction were given small doses of the drug by mouth as well, whereupon response began to appear and repigmentation took place.

Intradermal injections were also given to patients receiving general treatment without much benefit, to combine intradermal injection with the systemic treatment. The patches which refused to improve under general treatment were thus made responsive by means of intradermal administration of the drug. The oral medication used was tablets containing 10 mg. of Ammoidin and 5 mg. of Ammidin.

The paint is prepared to contain 7·5 mg. of Ammoidin and 2·5 mg. of Ammidin in each c.c.

Vitamin B complex was always prescribed with the treatment, either orally or parenterally together with a tonic containing iron.

Controls.—In patients under intradermal local treatment alone, some patches were used as control. These control areas were (a) not treated at all ;

(b) injected intradermally with the drug but not irradiated ; or (c) exposed to ultraviolet irradiation only. All control areas showed no tendency towards repigmentation. It was found necessary to combine ultraviolet irradiation with the intradermal injections in order to obtain the desired effect.

Reaction to the intradermal injections.—Immediately following the injections nothing more is seen than the usual appearance after an intradermal injection of any inert substance, showing prominence of skin pores and blanching of the injected area. Soon after the disappearance of this, the injected areas react with some erythema and oedema extending about half a centimetre around the puncture. This reaction is intensified by ultraviolet irradiation. The whole irradiated area reacts and remains red and slightly oedematous for a day or two. After subsidence of the diffuse erythema scaling may be noted, and the injection punctures remain erythematous for a longer period.

Sensitization phenomenon.—One patient (Case 12) showed a local sensitization reaction with vesiculation after the first set of injections. The reaction subsided with ordinary topical applications, and the drug was used no more. This patient had used the drug orally and as a paint two years previously.

Although the drug has been extensively used in the treatment of leucodermia, no case of sensitization has been reported after oral medication, and only very rarely after local painting. I have encountered only two cases of contact sensitization in practice.

Fifteen cases were studied, and particulars are given in Table I. Most of the cases were selected from among those who did not respond satisfactorily to the oral medication and local painting, or who showed only limited improvement.

Response to Treatment.

The response starts to appear after 3 to 6 weeks and two patterns of reaction were observed :

(1) *Perifollicular response.*—Tiny punctate pigmented perifollicular spots appear as a first sign of good response. These spots deepen in colour and enlarge in size, coalesce, and fill the vitiliginous areas. In this way complete cure of the area is obtained (Figs 1, 2, 3).

(2) *Marginal response.*—In a few patches the edge grows inwards until it reaches the few islets developed in the centre. It is an example of the marginal response described in previous papers (Figs. 4, 5, 6). This type of response was observed in some patches even where we were not limiting the injection to the periphery of the patch. It seems as if the central area away from the healthy skin has been severely repressed and its regenerative capacity is minimal. Both types of repigmentation may be seen in one and the same patient.

TABLE I.

Case No.	Age (years).	Duration of disease.	Size and sites of the lesions.	State of disease.	Treatment and irradiation.	Duration of treatment.	Response.	Results obtained.	Remarks.
1	35	1 year	2 patches 3 × 2 cm. on the R. leg.	Quiescent	Intradermal injections. U.V.R. once weekly. No drug given by mouth	2 months	Pigmented perifollicular spots began after the 3rd week	Complete cure	—
2	20	4 months	4 patches 1 × 1 cm. on the face and neck	Active	3 tablets daily; local paint; U.V.R.	1 month	No response		—
					Weekly intradermal injections added.	3 months	Repigmentation began after the 5th week	Ditto	
3	18	2 months	3 patches 2 × 1 cm. on the R. side of the face	,,	3 tablets daily; local paint; U.V.R.	1 month	Good response of one of the face patches		1 small patch appeared on the nape during treatment. It responded easily to injections.
			2 patches on the nape, 3 × 2 cm.	,,	Intradermal injections added.	2 months	Response began to appear after the 3rd week in all patches.		
4	16	3 months	5 × 3 cm. patch at the R. side of the nape	,,	3 tablets daily; local paint; U.V.R.	1 month	No response		½ × ½ cm. patch appeared on the neck and R. antecubital fossa after complete cure and responded easily to intradermal injections.
					Weekly intradermal injections added	3 months	Perifollicular pigmented spots appeared rapidly, fused and completely filled the patch	,,	
5	34	7 years	Large patches on trunk and limbs	Quiescent after activity	Oral medication; local paint; sun exposure	3 months	Slow progressive improvement of most of the patches		The large patches responded to oral and local treatment leaving 3 small patches which responded to intradermal injections.
					Weekly intradermal injections of the resistant patches and U.V.R.	3 months	Good response of the resistant patches	,,	

			Rt. Fr. forearm. 6 × 4 cm. R. ankle		Intradermal injections added once weekly	6 months	Rapid perifollicular pigmentation after the 4th week	Good	Complete cure of all patches except the ankle area which is still refractory.
7	20	7 years	2 elongated patches on both forearms reaching the elbows 9 × 2 cm. Large patches on the sides of both thighs 9 × 12 cm. Extensive areas on face	Quiescent	Weekly intradermal injections; paint; U.V.R. No tablets given	7 months	Good response to treatment after the 3rd week.	,,	Attendance of patient was not regular. The face lesions responded completely to oral medication and U.V.R. and the limbs only improved. The resistant areas responded promptly to intradermal injections.
8	30	5 years	Extensive lesions on both legs	Quiescent	Oral medication; paint; U.V.R.	3 months	No response	,,	Leg areas were not injected and did not improve.
		3 years	Large areas on both elbows		Weekly intradermal injections added	6 months	Rapid perifollicular pigmentary response		Small patches amidst the healed big areas did not improve.
9	23	3 years	Large patches on abdomen and thighs. Small patches on the arms. Resistant small areas amidst the healed large areas	Active	Oral medication paint; U.V.R.	6 months	Good response	,,	Good improvement of the big patches. Complete cure of the arm areas. Improvement of the refractory small areas.
					Intradermal injections added once weekly	4 months	Slow response		
10	12	10 years	7 × 5 cm. on the back	Quiescent	Oral and local medication and U.V.R.	6 months	No response	,,	Complete cure of the back lesions. The perifollicular spots in the calf area failed to unite. No response of the small areas.
			9 × 7 cm. on the left calf 3 areas 1 × 3 cm. on the R. leg		Intradermal injections added once weekly, and irradiation 3 times per week	3 months	Slow but progressive improvement		

TABLE I.—(*Cont.*)

Case No.	Age (years).	Duration of disease.	Size and site of the lesions.	State of disease.	Treatment and irradiation.	Duration of treatment.	Response.	Results obtained.	Remarks.
11	38	26 years	Big areas on the chest and sides of the neck	Intermittent phases of activity and quiescence	Oral and local medication and sun irradiation 3 years ago	10 months with periods of rest	Progressive improvement	Moderate result	Good response of the big areas. Partial improvement of the injected areas.
					Intradermal injections and U.V.R. added once weekly to resistant areas	3 months	Slow response		
12	37	12 years	Extensive involvement of arms and legs. Small areas on trunk and genitals	Quiescent	Oral and local medication and U.V.R two years ago. Intradermal injections given once	12 months with periods of rest	Very poor response	Failure	Only few spots appeared. Patient showed local sensitization reaction to injection. Treatment stopped.
13	19	11 years	Small areas on the face and neck.	Quiescent with periods of activity.	Oral and local medication and U.V.R.	6 months	No response	,,	—
			Large areas on the lateral aspects of the thighs		Intradermal injections added once weekly	3 months	No response		
14	22	12 years	Hands and fingers extensively affected	Ditto	Oral and local medication and U.V.R one year ago.	1 year with periods of rest	No response	,,	Partial improvement of the thigh areas.
			Small areas on the R. thigh and R. ankle		Intradermal injections and U.V.R. once weekly added	3 months	No response		
15	35	1½ years	One large area on the forehead. R. breast: area, 3×2 cm.	Active	Oral and local medication and U.V.R.	2 months		,,	Lesions of breast, side of the face and forearm improved.
			R. forearm: area, 1×1 cm.		Intradermal injections and U.V.R. added	4 months			

Results Obtained.

Out of the fifteen cases studied, five cases were considered cured, i.e., all the vitiliginous areas returned to normal. In five cases the response to treatment was considered good, i.e., certain areas treated were completely

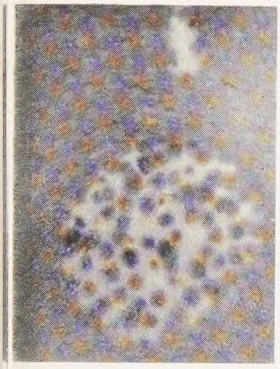

FIG. 1.

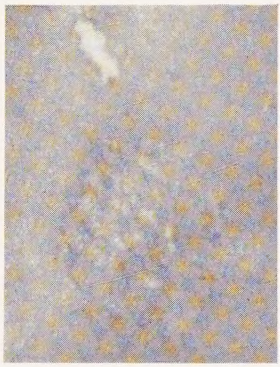

FIG. 2.

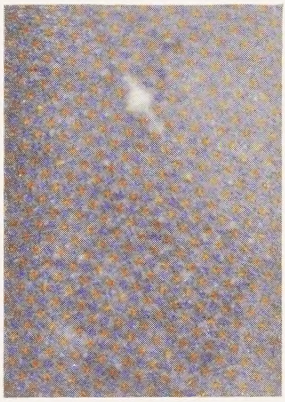

FIG. 3.

FIG. 1.—Perifollicular repigmentation. Soon after the beginning of treatment.
FIG. 2.—The same case later on.
FIG. 3.—The same case healed.

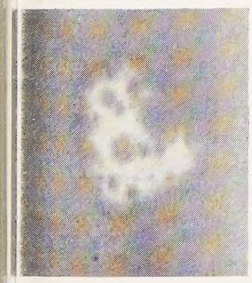

FIG. 4.

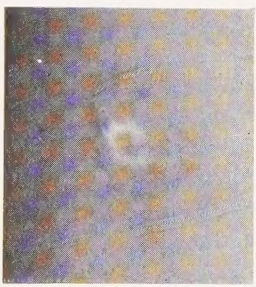

FIG. 5.

FIG. 6.

FIG. 4.—Marginal repigmentation. At the beginning of treatment.
FIG. 5.—The same case later on.
FIG. 6.—Completely healed.

cured, while other areas showed partial improvement. In one case the result was considered moderate, i.e., the case treated responded by partial incomplete pigmentation. The treatment was considered a failure when either very slight or no pigmentation appeared, or when the patient developed sensitization that necessitated stopping the treatment. In four of the cases studied the results were considered a failure.

Out of the 10 cases that have shown good response or complete cure after intradermal injections, five were refractory to oral administration of the drug continued for a sufficient time before intradermal medication was started. In two of the cases repigmentation was obtained only when the intradermal treatment was supplemented by oral administration of the drug.

None of the areas that were completely cured by the intradermal route became depigmented again.

The good results obtained were not limited to cases of short duration presenting small areas of leucoderma ; patients with extensive areas and of long duration have shown great improvement and good response.

In one case, where we had a moderate response to the treatment, fresh areas of vitiligo appeared while the treatment was being carried out in the old ones.

The control areas, untreated or treated by intradermal injections alone or by irradiation alone, failed utterly to show any tendency to repigmentation.

Disadvantages of Intradermal Medication.

Intradermal injection is a tedious way of treatment, and is not painless, especially in sensitive areas. It is more expensive than general treatment. If there is a tendency for the disorder to spread, general treatment is preferable.

Discussion.

Since the work of Bloch (1927) it has been repeatedly proved by various workers that the leucodermic skin is " dopa " oxidase negative and that the " dopa " reaction is a reliable indicator of the capacity of cells to form pigment. Epidermal sections taken from vitiliginous areas immersed in solutions of dihydroxyphenylalanin fail to show any pigment formation in any of the cells, in contrast to areas of normal skin which show increase of pigment in the melanoblasts. The idea held is that this failure of pigmentation is attributable to a temporary inhibition of the enzyme " dopa " oxidase, a copper-containing enzyme, now known to be identical with tyrosinase (Fitzpatrick *et al.*, 1950). In vitiligo tyrosinase fails to transform the amino acid tyrosine into dihydroxyphenylalanin, and the latter to melanin. This intracellular enzymatic change proceeds through intermediate reactions and molecular rearrangements to form melanin. There seems to be fair agreement that there are factors which inhibit and other which stimulate this process (Burn, 1951).

The skin contains under normal conditions certain substances which inhibit the action of tyrosinase (Rothman *et al.*, 1946). Aqueous extracts of human epidermis inhibit the oxidation of tyrosine and " dopa " and prevent the formation of melanin. This inhibitory action is mainly due to the SH groups contained in the skin. It has been proved that the power of the skin to inhibit

melanin formation has a certain mathematical relation to its SH content (Flesch and Rothman, 1948).

Ascorbic acid is another substance which will inhibit pigmentation. Being a reducing agent, it will inhibit the oxidation of tyrosine by tyrosinase, and it has been said that large doses of ascorbic acid will diminish pigmentation in Addison's disease. Exposure of vitamin C to ultraviolet rays or x-rays will oxidize it. It may be possible that together with sulphydryl compounds in the skin vitamin C may play a part in inhibiting melanin formation (Dowling and Whitlock, 1952).

Among common inhibitors of pigmentation are hydroquinones, succinylsulphathiazol, glutathiones and organic sulphur-containing compounds such as thiourea and thiouracil.

Solutions of these substances will inhibit *in vitro* the action of tyrosinase; the same occurs *in vivo* locally, e.g., industrial glove contact vitiligo (Oliver *et al.*, 1940), and generally, e.g., in treating thyrotoxicoses in negroes (Hellerstein, 1940).

Among the activators of pigmentation ultraviolet irradiation is a good example. It oxidizes the sulphydryl content of the skin, and so lowers it by about 20%. It also helps the transformation of the propigment dihydroxyphenylalanin into melanin. Reduced melanin can be oxidized to the darker form by exposure to ultraviolet rays. Among the activators are cupric ions, iron and arsenic. Pantothenic acid, folic acid, biotin and *p*-aminobenzoic acid have a stimulating effect on the process of melanogenesis (Lerner and Fitzpatrick, 1950). Depigmentation of the skin has been observed in children on multiple-vitamin deficient diets, pigmentation gradually returning after treatment with injectable liver extract, powdered stomach and full diets (Gillman and Gillman, 1945).

Hormones of the thyroid and pituitary, oestrogens and androgens play a great rôle in controlling melanin formation, both in normal and pathological conditions (Burn, 1951).

Under normal conditions a state of equilibrium seems to exist within the melanoblasts and the basal-cell layer of the epidermis between the sulphydryl compounds and the copper-containing enzyme. Any disturbance of this equilibrium by a reduction of the SH group will lead to activation of the enzyme to form pigment, and any rise of the amount of the SH groups will inhibit pigmentation.

This rapid progress in our knowledge concerning the physiology of pigmentation has shown the complicated nature of pigmentary disorders, and has pointed out the possibility of multiple mechanisms in the production of vitiligo. This has to be kept in mind by all workers in the field of therapeutic aspects of leucodermia. It seems that there are three different mechanisms that may play a rôle in the production of leucodermia.

I. *Failure of the Intracellular Enzymatic Process of Pigmentation.*

(1) The supply of the propigment dihydroxyphenylalanin, which is transformed into melanin, may be at fault. This seems a remote possibility.

(2) The enzymatic action may be at fault in various ways :

(*a*) The enzyme itself may be inactive, probably due to relative lack of copper, which has been proved to be essential for the activity of tyrosinase.

(*b*) In the presence of active copper-containing enzymes, the enzymatic process could be inhibited by certain inhibitors, e.g., sulphydryl groups.

II. Failure of the Melanoblast.

The melanoblast cannot be looked upon as an inert test-tube within which the enzymatic processes are carried out. Though all essential factors for enzymatic action may be available in a way sufficient for formation of melanin *in vitro*, yet this may not be achieved under certain conditions *in vivo*. It is well known that the enzymatic action can proceed *in vitro* without any need of the presence of vitamins or hormones, while *in vivo* intracellular melanin formation necessitates the presence of such substances. As an example, pigmentary response to ultraviolet light in castrated men fails to occur unless androgens are supplied, although intracellular enzymatic requirements are ensured (Edwards *et al.*, 1941).

Haxthausen (1947), in his graft experiments, has shown that vitiliginous skin transplanted into healthy areas succeeded in gaining normal pigmentation, while the transplantation of normal skin to vitiliginous areas caused the disappearance of pigment in the transplants. Some workers suggest that pigmentation depends on nerve supply ; others think that leucodermia cannot be totally explained by the mere failure of the enzymatic process or faulty nerve supply, and postulate changes in the biologic integrity of the cell.

It is feasible that melanogenesis could be profoundly affected by changes in the permeability of the cell membrane of the melanoblast, interfering with the chemical interchanges essential for successful intracellular melanin formation.

III. Melanin Destruction.

The pathology of leucodermia has always been thought of as essentially a failure of pigment formation. When we consider the problem on a broader basis we cannot ignore the possibility of melanin disintegration into colourless substances. That this can take place is beyond doubt. Certain foreign reducing agents, e.g., hydroquinones, have been found to act as poisons to induce melanin disappearance, as in occupational leucodermia. That this may be the case in vitiligo (idiopathic leucodermia) could be satisfactorily shown by the rapid rate of appearance of the depigmented areas, pointing to the

possibility of actual melanin destruction rather than failure of the enzymatic process of pigmentation to cope with the normal wear and tear of the skin pigment.

It is thus shown that the mechanisms through which leucodermia might be required are so many that it is hardly possible to expect any single line of treatment to be effective in all cases.

The results obtained with *Ammi majus* Linn. were so encouraging that we have come to the following conclusions :

(1) *Ammi majus*, when it reaches the sites of leucoderma by oral ingestion, by painting, or by intradermal injection, has a specific therapeutic action inducing repigmentation in a way not comparable with any other known treatment.

(2) *Ammi majus* has a local peripheral action at the site of the leucodermic area, being effective when applied intradermally. This renders the possibility of a general effect on the endocrine or nervous system rather remote. The mode of action of *Ammi majus* is still far from being clearly understood.

The observation that normal individuals, such as relatives of the patient, coming in contact with the drug may show excessive local pigmentation favours the assumption that the drug acts by stimulating melanogenesis rather than by inhibiting melanin disintegration. This phenomenon was also observed in patients when the drug came accidentally in contact with normal areas of their skin.

The results obtained in this work show that local application of the drug is a very effective way of treatment. The difficulties encountered during intradermal medication show that this way of local application is far from being the ideal method of treatment. A suitable penetrating vehicle ensuring prolonged and even local absorption of the drug is urgently needed.

I wish to express my thanks to the Memphis Chemical Company, Cairo, for the supply of tablets, paint and ampoules.

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THE TREATMENT OF ESSENTIAL HYPERIDROSIS WITH HEXAMETHONIUM BROMIDE: A PRELIMINARY REPORT.

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THE work of Kuno (1934) has established that there are two types of sweating, one due to emotional cause, the other thermal. Emotional sweating is most marked on the palms and soles but also occurs in the axillae and on the forehead. That the control of sweating is a function of the autonomic nervous system is now an accepted fact. Woollard and Phillips (1932) have shown that anatomically the nerve fibres supplying the sweat glands are distributed *via* the sympathetic ganglia to the post-ganglionic sympathetic fibres, which are finally distributed to the skin with the sensory nerves. Acetylcholine stimulates the secretion of sweat but atropine inhibits it. Accordingly, the nerve supply anatomically is sympathetic but its action physiologically is parasympathetic. Dale and Feldberg (1934) explained this anomaly when they demonstrated that the nerves exciting the sweat glands are cholinergic. Acetylcholine is liberated and acts as the chemical transmitter for the impulses to the sweat glands, whereas the majority of the sympathetic nerve fibres innervating other structures are adrenergic, adrenaline and *nor*adrenaline being the chemical transmitters. In an attempt to clarify the excessive sweat secretion in essential hyperidrosis, Chalmers and Keele (1952) were not able to demonstrate either hypersensitivity to acetylcholine in the sweat glands or reduced cholinesterase activity. It seems likely therefore that the excessive sweating in such cases must be due to an *excess* of acetylcholine liberated in response to stimuli arising centrally. Earlier work by Chalmers and Keele (1951) has shown that sweating on the forearms and palms can be induced by the local injection of adrenaline and *nor*adrenaline, thus confirming the work of Haimovici (1950) and Sonnenschein *et al.* (1949). They were unable to produce inhibition of sweating by locally introduced adrenalin antagonists. Shelley (1951) showed that the apocrine sweat glands of the axilla could be stimulated by adrenaline and their sweating inhibited by adrenaline antagonists, though not by atropine. Acetylcholine did not excite the apocrine sweat glands. Thus it seems feasible that while the majority of the sweat glands are controlled by the cholinergic nerve fibres of the sympathetic system, the apocrine sweat

glands are controlled by adrenergic fibres. This brief survey of the nervous control of sweating would seem to suggest that in attempting to control essential hyperidrosis the aim should be to interrupt as centrally as possible the transmission of impulses by acetylcholine. The ganglia of the autonomic nervous system seem to be a suitable target for such an attempted block.

The action of the quarternary ammonium compounds in blocking the transmission of impulses through the autonomic ganglia was noted by Burn and Dale (1915) and again by Hunt (1926). The pharmacological studies of Acheson and Moe (1945, 1946) and Lyons *et al.* (1947) led to a search for orally active ganglion blocking agents with prolonged effect. The simultaneous publication by Paton and Zaimis (1948) and by Barlow and Ing (1948) of the ganglion blocking effects of the polymethylene bistrimethylammonium compounds (alkamethoniums) further stimulated this search. After Paton and Zaimis (1948) had noted the clinical potentialities of the penta- and hexamethylene members of this series they later (1949) showed that their pharmacological properties are as follows: The site of action is at the preganglionic synapse, the blocking effect being apparent at both sympathetic and parasympathetic ganglia, and is related to the length of the polymethylene chain, being most marked in the penta- and hexa- members of the series. The same observers (1951) showed that this ganglion blocking effect takes place without initial excitation: in clinically applicable dosage it is without neuromuscular blocking effect, has no muscarine-like action and no histamine liberating effect. They further observed that the effect of these alkamethonium drugs is more marked on abnormally excited structures than on structures in physiological equilibrium. Burt and Graham (1950) when testing penta- and hexamethoniums in hypertension and peripheral vascular disease noted that sweating is reduced in normal subjects, and in a case of hyperidrosis the excess sweating was rapidly controlled. Tolerance developed rapidly in this case, however, and treatment was discontinued.

The results reported below were obtained by treating cases of localized (essential) hyperidrosis with hexamethonium bromide (hexamethylene 1:6 bismethyl ammonium bromide). The trial was prompted by the currently accepted concept of the nervous control of sweating and by the isolated finding of Burt and Graham referred to above.

The treatment of localized hyperidrosis has been a vexed question in the past and mention is made here of some of the methods employed. Local astringents have been used, but their effects have been found to be temporary and incomplete. Sedation with bromides and barbiturates is of value in very mild cases but their use is somewhat limited. Atropine has long been used, but in effective dose is usually accompanied by inhibition of salivation and disturbance of accommodation. Grimson *et al.* (1950) report good results using Banthine (β-diethylaminoethyl-xanthine-9-carboxylate methobromide), but it

does not appear to be much superior to atropine, having similar side effects. The exposure of affected areas to x-rays has given good results, but as the dosage required to inhibit sweat-gland activity is high the method is not without risk of permanent damage to the skin. Surgery of the sympathetic ganglia is also not without operative risk and residual effects such as Horner's syndrome outweigh its advantages. It has also on occasion been followed after a time by a severe recurrence of the hyperidrosis. Operative procedures therefore fall into the category of last choice treatments.

Six cases of localized essential hyperidrosis were treated with oral hexamethonium bromide. The cases treated were moderately severe or severe examples of the condition and had resisted previously attempted control with astringents, sedation and atropine. All six cases were admitted to the wards, and after full investigation to exclude organic disease treatment was commenced. Hexamethonium bromide was given in 250 mg. tablets and the dose gradually increased to 1250 mg. daily, spread over the waking hours. When clinical improvement was achieved and when it was evident that no toxic effects had occurred the patients were allowed home to attend as out-patients. Base-line blood-pressure recordings with the patient in bed and ambulant were made prior to treatment; these were continued after commencement of treatment up till dismissal.

In only one case was there any significant fall in blood pressure. This patient had a hypotensive attack with nausea and vomiting, occurring while at rest in bed taking 750 mg. hexamethonium bromide daily. The drug was withheld, the patient allowed up, treatment recommenced and the dose gradually increased to 1250 mg. daily with no further evidence of intolerance. A temporary tachycardia was the only manifestation of intolerance when the patient was ambulant, and this disappeared in less than 24 hours. No case showed visual or salivary disturbance. The case with the hypotensive attack was the only one with any gastric upset and this upset has been attributed to the fall in blood pressure.

In all six cases the hyperidrosis was controlled initially and the minimum period of control was two months. A transient return of sweating in the early hours of the morning was noted by all six. This was not unexpected, as treatment was not continued throughout the night. The effect, although considerable, was not as complete in the axillae as on the palms and soles. Two cases were controlled for periods of three and four months respectively by 1250 mg. daily and have remained controlled for five months after the drug was stopped. One case controlled by the same dose for two months defaulted and all efforts to find her were in vain. Two cases controlled for just over two months on 1250 mg. daily experienced partial relapses while still on treatment. They had transient returns of sweating with intervening periods of control. Both patients maintain, however, that the hyperidrosis when present

is less severe than formerly. It must be assumed that these cases are developing tolerance to the drug.

The remaining case was controlled for just over three months by 1250 mg. daily when treatment was stopped on account of an exacerbation of chronic bronchitis. When treatment was recommenced a month later only partial control was achieved. It is felt that tolerance is developing in this case, but it should be noted that the patient is elderly and unco-operative and carries out her treatment in a haphazard, somewhat absent-minded fashion.

Thus, all six cases were initially controlled, two apparently indefinitely and without further treatment, one defaulted while controlled and has not been seen since, and three have apparently tended to develop tolerance. Full details of these cases are revealed in the table.

TABLE I.

Sex.	Age.	Duration of hyperidrosis.	Degree of severity.	Distribution of hyperidrosis.
F.	19	1 year	Severe	Hands and axillae.
M.	22	3 years	,,	Hands and feet.
F.	18	Lifelong	Moderate	,, ,,
F.	57	,,	Severe	Forehead and hands.
F.	18	6 years	,,	Hands, axillae, forehead.
F.	17	5 ,,	Moderate	Hands and axillae.

TABLE II.

Daily dose.	Duration of treatment.	Duration of control.	Remarks.
1250 mg.	4 months	9 months	Controlled 5 months without further therapy.
,,	3 ,,	8 ,,	Controlled 5 months without further therapy.
,,	2 ,,	2 ,,	Defaulted whilst still controlled.
,,	4 ,,	3 ,,	Controlled 3 months; off 1 month; partial control 1 month. ? Tolerance.
,,	4 ,,	2 ,,	Control 2 months; partial control 2 months. ? Tolerance.
,,	4 ,,	2 ,,	Ditto.

Since the institution of this trial Chalmers and Keele, whose clarification of some of the factors in the nervous control of sweating was referred to earlier, have controlled four out of six cases of hyperidrosis with 750 mg. of hexamethonium bromide daily. The results of the present series are fairly similar, but in none of the cases was 750 mg. daily sufficient to control sweating.

From such a small group of cases as this it would be unwise to draw any conclusion, but the result obtained in this preliminary investigation has stimulated further and fuller research into the possible role of ganglion blocking agents in the control of localized hyperidrosis. The results of these later investigations will be published in the near future.

Summary.

1. The current views on the nervous control of sweating are outlined.

2. A brief survey of the pharmacology of the alkamethonium group of drugs is made.

3. Various treatments of localized hyperidrosis are mentioned.

4. The results of treatment of six cases of hyperidrosis treated with hexamethonium bromide are recorded.

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A SEROLOGICAL REACTION OBSERVED IN CERTAIN CASES OF BULLOUS DERMATOSES.

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In the course of an investigation into an agglutination reaction observed in red cells incubated with skin extracts, specimens from a case of advanced pemphigus vulgaris were submitted. It was noted that the skin fragments were excessively greasy, and the fat was consequently extracted with ether before proceeding with the experiment. This ether extract, however, was not discarded: instead, an alcohol antigen was prepared from it and a strong flocculation reaction obtained with the patient's serum. As the extracted fat was predominantly derived from the patient's dressings, an extract of soft paraffin was prepared and used in the same way. The same flocculation reaction was noted with this and with a second sample of yellow soft paraffin (paraffinum molle flavum) obtained from the hospital.*

Further tests were made with the sera of patients suffering from various diseases, chiefly cutaneous, and from adequate normal controls; they have shown flocculation only in cases of pemphigus and dermatitis herpetiformis: in the latter only such as showed or had shown bullous lesions were positive.

METHOD.

1. 10 mg. of commercial yellow soft paraffin is dissolved in 10 c.c. of ether and evaporated to dryness. The residue is suspended in 5 c.c. of absolute alcohol and stirred constantly at 56° C. to effect solution. This solution is filtered at 56°.

2. To 0·2 c.c. of the filtrate, warmed to 56°, is added 0·02 c.c. of warm 1% cholesterol. 2 c.c. of warm normal saline is poured rapidly on to the mixture: the resultant turbid cholesterinized antigen is used in the test.

3. Sera are inactivated at 56° for half an hour.

4. Two tubes of serum are set up for each test. Each contains 0·1 c.c. of inactivated serum: one contains in addition 0·1 c.c. of antigen, the other 0·2 c.c.

5. The tubes (along with controls similarly treated) are placed on a mechanical shaker for 10 minutes and results read immediately as a flocculation reaction. Reactions are entered as + to ++++, graded in the same way as results of the Kahn flocculation test.

In stages 1 and 2 the alcoholic solution must be warmed to 56° to retain solution of the vaseline extract, and for the same reason pipettes used in the next stage are rinsed with alcohol warmed to the same temperature.

* Manufactured by the Standard Oil Company, New Jersey.

Results.

Positive reactions have been obtained in the following cases :

No.	Sex.	Age.	Disease.	Duration of disease.	Result.	No. of tests.
1	M.	49	Pemphigus chronicus vulgaris	3 years	++++	5
				+ 3 months	+++	1
2	F.	65	Dermatitis herpetiformis	3 years	++	1
3	M.	60	Pemphigus chronicus vulgaris	2 ,,	++	2
4	F.	45	,, ,, ,,	2 ,,	++	2
				+ 2 months	+++	1
5	M.	28	Dermatitis herpetiformis	6 ,,	+	1
6	F.	62	,, ,,	8 ,,	+	1
7	M.	30	Pemphigus chronicus vulgaris	6 ,,	+	1
				+ 1 week	++	1
				+ 2 weeks	++	1
8	M.	66	,, ,,	1 year	Neg.	3
				+ 6 months	+	1
				+ 7 ,,	[illegible]	1
9	F.	60	Pemphigus vegetans	3 weeks	Neg.	1
				+ 3 ,,	Neg.	1
				+ 5 ,,	+	1
				+ 6 ,,	+	1
				+ 8 ,,	+	1
10	F.	28	Herpes gestationis (bullous dermatitis herpetiformis of pregnancy)	4 weeks	Neg.	1
				+ 3 ,,	+++	1

It will be noted that in Cases 8, 9 and 10 the reaction became positive during the course of the disease. In Case 7 the reaction became stronger. Case 4 was a Negress ; the others were whites.

Negative reactions were given by the sera—

(i) Of one patient who has had 3 years' complete remission, without treatment, from pemphigus vegetans ; from a second with 5 years' complete remission from dermatitis herpetiformis.

(ii) Of patients with the following bullous eruptions : erythema multiforme bullosum, epidermolysis bullosa acquisita with porphyria, disseminated lupus erythematosus with bullous lesions, erythroderma ichthyosiforme with bullous lesions, acute tinea pedis.

(iii) Of patients with the following non-bullous eruptions : dermatitis herpetiformis with papulo-vesicular lesions only (3), endogenous eczema (2), contact dermatitis with auto-sensitization (2), psoriasis (2), so-called lipomelanic reticulosis (2).

(iv) Of patients suffering from infective hepatitis, viral pneumonia and peripheral neuritis.

(v) Of 10 subjects reported as "positive" by the Wassermann laboratory.
(vi) Of 71 presumably healthy blood donors.

An antigen prepared in the same way, but from lanolin (adeps lanae anhydrosus), did not give a flocculation reaction with the sera of Cases 1 and 2.

Discussion.

The intensity of the reaction has been roughly proportional to the severity of the disease in this small series. Thus Case 1, who has consistently given the strongest reaction, was moribund before cortisone could be obtained, with denudation of 70% of the body surface. After progressing to complete freedom from clinical manifestations of pemphigus, his serum continued to give a ± ± ± − reaction for a further 3 months; after a further period of 3 months, however, the reaction became less marked (+++).

Case 9 gave a negative result while lesions were confined to the mouth and vulva, and became consistently positive 3 weeks after bullous and vegetating lesions developed on the skin. Case 8 was negative after a year of moderately severe typical pemphigus vulgaris, while reasonably well controlled with cortisone. He suffered a severe relapse soon after discontinuing maintenance therapy, and on readmission gave a + reaction which became ++++ a month later, even though the disease had by that time again been brought under control clinically.

There was no common drug factor. Several of the patients were on cortisone therapy, but others (Cases 2, 5, 6, 7) had not been given this hormone. On the other hand, several of the negative reactors from groups B (ii) and (iii) were taking cortisone when their sera were tested.

Attempts to incriminate some known alteration in the blood chemistry have been unsuccessful. No connection could be found with changes in serum electrolytes or proteins. Indeed, in the case of a patient dying of liver failure accompanying infective hepatitis the grossest changes in blood chemistry were found; there was, however, no flocculation with the paraffin antigen.

The reaction does not apparently follow on the production of bullae in the course of other diseases. Nevertheless the number of cases in group B (ii) is still too small for firm conclusions to be drawn.

We do not believe that the flocculation reaction represents the formation of antibodies to externally applied soft paraffin. Apart from the fact that such a serological response would be almost unique, it is pointed out that Cases 2, 3, 7 and 9 had no history of any such external application; many of the patients in groups B (i), (ii) and (iii), on the other hand, had received dressings and inunctions with topical remedies in a paraffin base, without exhibiting the flocculation reaction.

The flocculation reaction appears to show some specificity, in so far as it was positive in all 10 cases of a series of pemphigus and bullous dermatitis herpetiformis and negative in over 100 controls. It appears, however, from Cases 8, 9 and 10 that the disease must be well established before the reaction becomes positive, hence it is unlikely to be of value as an early diagnostic test, at least in its present form.

Leaving aside the question of immediate practical applications, however, we feel that this phenomenon deserves further study. It is possible that more light may thus be thrown on the biochemical changes occurring in these imperfectly understood diseases. A possible approach, which we intend to use, is the fractionation of soft paraffin: in this way it might be possible to determine which of its component hydrocarbons is or are responsible for the observed phenomenon.

Summary.

A serum flocculation reaction is described, which has been positive in 10 cases of pemphigus and dermatitis herpetiformis with bullous lesions, and negative in over 100 controls.

We wish to thank several colleagues, especially Dr. E. K. Dunning of the Johannesburg General Hospital, for their help in procuring material for this investigation.

MILKER'S NODULES. GROWTH OF THE VIRUS IN DEVELOPING HEN EGGS.

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Although the so-called milker's nodule has been known for over fifty years, it has often been doubted whether it is an aetiological entity. Certain clinical and experimental evidence has suggested that it differs from cowpox and vaccinia (Bonnevie, 1937), and the electron microscope has revealed a virus which is not that of vaccinia (Puntigam and Orth, 1951). We report here the isolation of the causal agent of milker's nodules on developing hen eggs and the results of inoculating this material into man and animals. These observations confirm the specificity of a virus causing at least some cases of typical milker's nodules.

Recent accounts of the clinical and histological features of milker's nodules have been given by Richter and Kressmann (1950) and Sonck (1951). Fasquelle *et al.* (1951) are apparently the only workers who have tried, albeit unsuccessfully, to grow the virus on the chorio-allantois of hen eggs. Their cultures were discarded on the third day, which was sufficient time to exclude the presence of one of the pock viruses (Downie, 1939; Dekking, 1950; Downie and Haddock, 1952), but perhaps too soon for the lesions of milker's nodules.

Observations.

Case history.—Two European farmer's daughters aged 14 and 16 complained of multiple nodules on the hands of two weeks' duration. These nodules were about 1 cm. across, some dome-shaped and others umbilicated grey brown in colour, with no clinical signs of vesiculation, exudation or ulceration. There was no lymphangitis, regional adenopathy or general exanthem. These lesions on the hands persisted for about six weeks and healed with scars that were barely visible. Both girls had been vaccinated against smallpox in infancy and the marks were still to be seen. A second vaccination six years ago was said to have taken. They were both revaccinated and a 48-hour papule (immune take) was produced. The girls were otherwise healthy, but they came from a large, impoverished family and were probably malnourished. For several months they had been milking cows with a disease of the udders. The district veterinarian found lesions on the teats in two of four cows. The lesions consisted of irregular superficial erosions 1–2 cm. in diameter covered with yellow crusts. All the animals were badly underfed and tick-infested.

One of the human lesions was excised for histological and virus studies.

Histology of the human lesion.—The epidermis showed acanthosis, absence of the

granular layer, parakeratosis and considerable elongation with branching of the rete pegs. At the tops of the papillae the basement membrane was disrupted by oedema and invasion of lymphocytes, fibrocytes, eosinophils and erythrocytes. Exudate containing these cells and their debris was present between the superficial parakeratotic layers. Spongiosis was seen, but no primary acantholysis. The papillary layer of the corium contained a dense cellular infiltrate consisting chiefly of lymphocytes, with histiocytes, fibroblasts, fibrocytes and eosinophils present in addition. Capillaries were prominent and swollen, with perivascular oedema but no frank haemorrhage. Lymph spaces were dilated. Haematoxylin and eosin, Giemsa, Gram, carbol acid fuchsin-light green, periodic acid-Schiff and Mallory's stains were applied, and no inclusion material was seen.

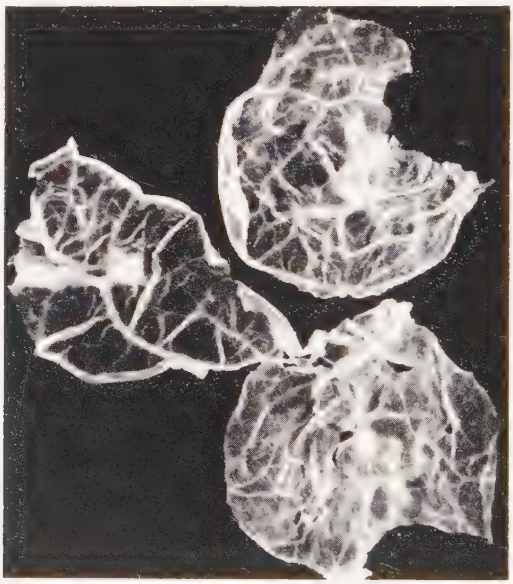

FIG. 1.

Cultivation in developing eggs.—A portion of the excised nodule was ground, suspended in a few ml. of broth and lightly centrifuged. After the addition of streptomycin and penicillin this material was placed on the chorio-allantoic membranes of twelve 8-day-old embryos, and the eggs were re-incubated at 35° C.

Five days later the eggs were opened and the membranes were seen to be somewhat thickened and oedematous at the site of inoculation. These portions of the membranes were collected and used to infect other eggs. In this way eight serial passages were made at intervals of 5 or 6 days. Only occasional deaths were observed. The ninth transfer was made to 12-day-old embryos, and the lesions on the third and fifth days were identical with those produced on the younger embryos.

Macroscopic changes in the membranes were not marked. They were oedematous and showed a few diffuse light grey areas. Fig. 1 shows the membranes from the eighth egg generation.

Microscopic examination was made of membranes from the first, third, seventh and eighth passages. In sections of the grey thickened areas, ectodermal proliferation was seen with active mitosis. The cells were swollen, with cytoplasmic vacuoles

FIG. 2.

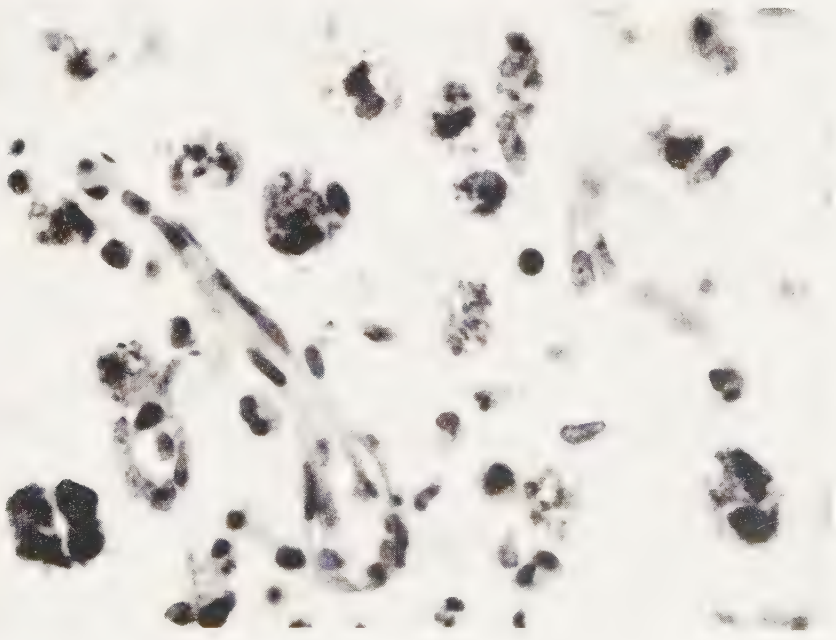

FIG. 3.

varying in size and number, and many of the nuclei also showed watery imbibition. Towards the surface of the thickening the ectodermal cells became hyalinized and the nuclei flat and pyknotic. Downward extensions of the ectoderm produced the appearance in some lesions of buried epithelial nests in the mesoderm. In certain areas the epithelium had sloughed. Among the cells of the ectoderm and on its outer aspect there were red cells, reticular cells, eosinophils and exudate which had permeated from the mesoderm.

The mesodermal reaction was variable. In some lesions there was little underlying mesodermal change, while in those where the epithelium had separated only a dense proliferation of spindle-shaped mesenchymal cells was seen. In its most developed form (Fig. 2) the mesodermal change consisted of an oedematous and cellular infiltrate of the outer half of the chorio-allantoic membrane. Capillaries were swollen and increased in number. The cellular infiltrate consisted mainly of eosinophils and reticular cells resembling fibroblasts, and to a less extent of adventitial and smaller lymphocyte-like cells. Myelopoietic changes were evident. There was emigration of a few red blood cells, but no frank haemorrhage. The reticular and adventitial cells showed vacuolation with some basophilic granulation of the cytoplasm. In some preparations (Fig. 3) the reticular cells were considerably distended by large cytoplasmic globules of varying size along with less well organized granular masses consisting of the same type of material. This substance was contained in vacuoles which compressed the cell nuclei. It appeared yellow with a slight bluish tint in haematoxylin and eosin preparations, and scarlet with the periodic acid-Schiff stain. It stained a faint blue-green with the Gram stain, but with Giesma stain it appeared a bottle green and showed areas of much greater density within the globular material. The origin and fate of this substance could not be decided.

Inoculations with chorio-allantoic material.—Chorio-allantoic membranes from the 7th egg generation were macerated, and after light centrifugation the supernatant fluid was used undiluted for human and animal inoculations.

(a) *Human.*—The fluid was inoculated by the scratch technique into the skin of previously variola-vaccinated adult male and female volunteers without producing any prompt or delayed effects. Intradermal injection of 0·2 ml. of the fluid in a male volunteer produced no changes that were not also seen with a control injection made from uninfected membrane.

(b) *Rabbit.*—Both eyes of two rabbits were cross-hatched with a hypodermic needle and 0·25 ml. of membrane material was then instilled into the left eye of each rabbit. They were examined daily for two weeks, but no corneal lesions were observed.

(c) *Bovine.*—The skin of the tail folds of two Afrikander *bulls* was scarified and then rubbed with swabs steeped in membrane suspension. An intradermal injection of 0·25 ml. of the fluid was given at the same time. Only a slight hardening of the skin at the site of the injection resulted. A Friesland *cow* which was in rather poor condition was chosen and two scratches of about 3 cm. were made down the length of one teat. Membrane suspension was then rubbed in with a swab. Six days later it was noticed that the lines had become prominent and red, and that a yellow crust was present over the length of the lines and extended about 3 mm. to each side. The following day a portion of one lesion was excised for histological examination. The lesions then gradually receded and by the 13th day had almost entirely disappeared.

Histology of the bovine lesion.—On either side of the scarification there was a crust representing an old subcorneal pustule. At the inoculation site there was a slight parakeratosis with some lymphocyte, fibrocyte and polymorph invasion of the epidermis, and a dense accumulation of polymorphs and fibrocytes in the dermis. There was a diffuse reaction around the vessels in the mid-cutis, where oedema and infiltration with histiocytes, fibroblasts, eosinophils and lymphocytes were noted. The histiocytes and vascular endothelium showed large quantities of fine basophilic material in the cytoplasm.

Summary.

Milker's nodules are reported for the first time from South Africa.

The chorio-allantoic membrane of developing hen eggs was successfully infected from a human nodule. A slowly evolving poorly circumscribed lesion was produced which differed from the egg lesions of vaccinia and cowpox. No constant inclusions were seen, but in certain lesions of the chorio-allantoic membrane a striking substance was noted in the mesenchymal cells.

Using infected membrane material a cow was successfully inoculated, but experimental transmissions were otherwise unsuccessful although the material was still infective to other incubated eggs. It seemed that this high natural resistance to infection might be lowered by a poor state of nutrition. Close general similarities in the pathological changes of human, bovine and egg tissues supported the aetiological unity of the lesions.

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THE TREATMENT OF POST-ACNE SCARS WITH PHENOL.

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ALTHOUGH no method has yet been devised that will eradicate post-acne scars, there are a number of procedures that may effect improvement. Of these phenol has given us the best results. (One of us - G. M. M. has been using it for this purpose since 1903). We employ phenol liquefactum U.S.P. When this is applied to the skin there is an immediate severe burning sensation, which endures about 45 seconds. During this period the skin assumes a milk-white colour. At the end of about 10 minutes the burning sensation returns and lasts intermittently for about 45 minutes, although it may be 60 to 90 minutes before there is complete comfort. Thereafter there is no pain at any time—only a tight dry feeling for the next 5 or 6 days.

When the phenol is applied there is almost immediate coagulation of albumen, which apparently prevents penetration and absorption. When applied to the entire face at one sitting there is no systemic phenol reaction that can be detected clinically or by laboratory methods. In a number of our patients urine tests, blood chemistry and phenol evaluation in blood and urine were done before and after treatment. No essential changes in any case were noted. Occasionally the conjugated phenols, of low toxicity, were slightly increased. This might be caused in various ways, one of which is a breakdown of the coagulated proteins of the skin.

The technique is as follows: The face is cleansed with soap and water. Castor oil is instilled under the eyelids. Before beginning the treatment one should have at hand a pledget of cotton wet with alcohol in case of accidental phenol contact. With a cotton applicator phenol is applied to one cheek rapidly, so that the entire cheek is treated as simultaneously as possible. After 30 to 60 seconds 95% alcohol is applied freely. The same procedure is repeated for the other cheek, the chin and the forehead. When in doubt about toleration treatment may be staggered, i.e., phenol is applied in the usual manner and its action checked in 2 or 3 seconds. If the reaction is normal (slight erythema) phenol is again applied and allowed to act for 5 or 10 seconds, and so on. By this procedure one can obtain the desired degree of reaction. The colour of the skin changes from white to grey-brown, and finally to red: each day, as the redness decreases, the skin becomes darker. There is moderate oedema, which may last 5 to 6 days. Exfoliation begins on the 4th or 5th day

and is complete by the 6th or 7th day. This exfoliation involves only the superficial layers of the epidermis. There is never vesiculation, bleeding or exudation.

To alleviate the severe burning sensation, different methods of local anaesthesia were tried without complete satisfaction. Injections of procaine hydrochloride gave good results, but most patients prefer the treatment pain to that of multiple injections. In some instances demerol hydrochloride or a morphine derivative was administered into the arm subcutaneously. This reduces the pain by half.

Patients are advised to stay indoors until the exfoliation is complete. During this period the face is not washed but is dusted with talc frequently. On the 5th or 6th day warm mineral oil is applied for 2 hours, followed by steaming with hot towels. The dead portions of the epidermis now exfoliate in large flakes, leaving the skin smooth and pink. Twice daily, for about two weeks, Intraderm Tyrothricin or a similar remedy is now applied. A sun-protective cream or lotion should be used for a month, and exposure to sunlight, direct or reflected, should be avoided.

Because of the possibility of depigmentation we did not treat coloured persons, but there has been no depigmentation in the ordinary brunette range. We do not treat patients with skin diseases other than acne, those allergic to phenol or coal tar, and patients with constitutional disorders such as nephritis, severe anaemia, tuberculosis or diabetes. We are cautious with patients who have had x-ray treatment: the first treatment is mild. However, many of the patients had received a full course of x-ray treatments (75 r once weekly for 16 weeks), yet their skin tolerated applications of full strength.

We have not encountered phenol allergy, sensitization, or any permanent untoward results. One patient had hyperpigmentation following acute sunburn a week after her first treatment. It lasted several months. Two others developed pigment at the borders of the application, also after exposure to the sun's rays too soon after treatment. The treatment has not caused keloids, ulceration, sloughing or infection in any of the 112 patients with a total of 540 treatments over a period of 10 years. Many private patients, who received the phenol treatment years ago, have been seen by the senior author 10 to 30 years later. There have been no late sequelae such as atrophy, hypertrophy, wrinkling, hyperkeratosis or epithelioma.

Every patient shows definite improvement. At times two to four treatments suffice. It is customary to allow an interval of two months between treatments. Most patients were improved 80%.

Histopathology.

Microscopical examinations were made one half-hour to two months after mild and strong applications. The two photographs show the results of one such study.

H. L—, male, received 6 monthly phenol applications to the right side of the upper part of the back. A biopsy was taken a month after the last treatment. Simultaneously, a biopsy was taken from a corresponding area on the untreated left side. Serial sections were stained with haematoxylin-eosin and Weigert's elastic tissue stain.

Untreated skin. The horny layer is thin and consists of loose lamellae. Throughout most of the section the granular layer consists of one or two rows of cells. The

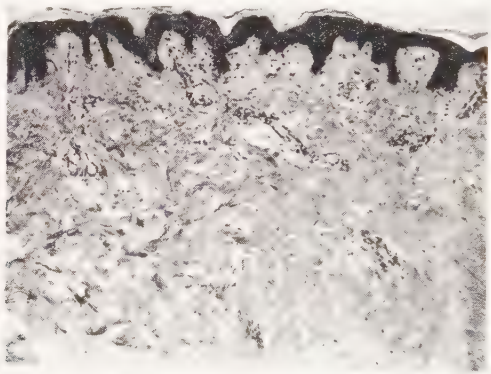

FIG. 1.

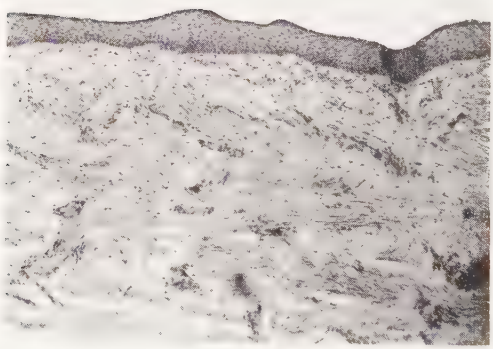

FIG. 2.

epidermis is thin. The rete pegs are short and the papillary bodies are broad. In the dermis the capillaries and superficial vessels are slightly dilated. The intima nuclei are regularly arranged and not enlarged. The collagen bundles and the appendages are normal. The elastica consist of fine, dark-staining fibres at the epidermodermal junction, becoming coarser lower in the cutis (Fig. 1).

Treated skin. The epidermis is flattened with obliteration of many rete pegs and papillary bodies. It is slightly thickened. The horny layer is thin and composed of loose lamellae. The granular layer has from two to four rows of cells. The basal cell layer is well defined.

The collagen bundles in the dermis are much denser and more compact than normal and are arranged more nearly parallel to the epidermis, especially in the upper corium

There are many scattered fibroblasts, particularly in the upper, and to a less extent, in the mid-corium. There are numerous small, thin-walled, dilated vessels in the upper and mid-cutis. In some instances their intimal nuclei are prominent and the lumens filled with erythrocytes. The capillaries of the sub-epidermal zone are very small and sparse. There is a slight infiltration of small round cells about some of the vessels. In the sections examined there were no follicles or sebaceous glands ; one small cluster of sweat glands was noted. The fine elastic fibres of the upper corium are absent. The coarser fibres of the mid- and deep corium are present and, apart from some fragmentation, reveal no abnormalities (Fig. 2).

Explanation of Results.

A combination of several factors may be responsible for the improvement. One factor may be an inherent quality that favours maximum response. Another may be improved circulation and physiological activity effected by the inflammation. A third factor may be the exfoliation, which is presumably most pronounced at the margins of the pits. It is probable that the principal factor is the change in the true skin, consisting mainly of collagen hyperplasia and a more horizontal arrangement of the collagen bundles. This may cause elevation of the floor of the pits. However, more experimentation is necessary before the question can be answered with complete satisfaction.

We are indebted to Dr. Maurice Bruger for the biochemical work, to Dr. Charles Sims for his study of many serial sections, and to Dr. Max Jessner for help with some of the histological material and for clinical opinions.

ROYAL SOCIETY OF MEDICINE.

SECTION OF DERMATOLOGY.

President—Dr. G. B. Dowling.

20 March 1952.

Febrile Relapsing Nodular Non-suppurative Panniculitis (Weber-Christian).—Dr. J. E. M. Wigley and Dr. O. L. S. Scott.

Married woman, aged 43. Admitted to hospital in February 1952, under the care of Dr. R. A. Hickling. She has suffered from vague ill-health for the past four years,

Fig. 1.—Weber-Christian disease, showing distribution of nodules on left leg.

which has been more noticeable in the past two years. Nine months ago she developed sharp pain in the right subcostal region, and this was followed within four weeks by the appearance of lumps on the legs. Since then other lumps have appeared on all four limbs, buttocks and chest, and they have tended to appear in crops. She has also suffered from diarrhoea and fever during this time. The former has been shown to be due to steatorrhoea. Histology of a recent subcutaneous nodule has been reported upon by Dr. H. Haber, who considered it to be consistent with a diagnosis of Weber-Christian syndrome, and drew our attention to a fatal case described by Bjornstad which had some similar features.

The disorder consists of recurring episodes of fever and the appearance of numerous tender, often painful, subcutaneous nodules. The nodules consist of non-suppurative inflammation and necrosis of the subcutaneous fat and other regions. The title "relapsing, nodular, non-suppurative panniculitis" was proposed by Dr. Parkes Weber in 1925 when he showed a case to the Association of Physicians in Belfast. In 1928 Christian rightly added the adjective "febrile" when he described his case which relapsed ten times in five years. Since then 44 cases have been reported. Its importance lies in the fact that it may pass unrecognized, may lead to severe disability, and in 6 cases it has terminated fatally.

The nodules in this case appear, as typically, in crops. At first they are only palpable and tender, later become red and visible, then darker red, brown and scaling, and finally in some cases break down and ulcerate (Fig. 1). If there is no ulceration the nodule heals with a puckered scar. This patient has had a low-grade fever for the past three months which rises to about 100 F. at night. She has lost about 2 st. (6·4 Kg.) in weight.

The interesting features of this case are the blood counts and the steatorrhoea. She has a macrocytic anaemia with moderate anisocytosis, poikilocytosis and polychromasia (Hb 79%, R.B.C. 3·6 million per c.mm., C.I. 1·09). This state of affairs has been found in several other cases, and may be explained by the fatty degeneration and necrosis of the liver that has been seen in 4 cases post mortem.

Her steatorrhoea is due to failure of absorption of split fat (split fat 56, unsplit fat 8, total fat 64 grammes % of total dry weight). This symptom has not been noted in other cases but it is probably caused by involvement of the intestinal wall and mesentery. These regions showed necrosis of fat and infiltration with macrophages in the case reported by Mostofi and Engleman (1947) at post-mortem, and our patient may be similarly but more severely affected.

Finally, the white blood count shows changes suggestive of glandular fever or lymphatic leukaemia (W.B.C. 15,100: neutros. 30·5, lymphos. 54·5, monos. 15%). We are unable to account for this.

Treatment has not yet been started, but it is proposed to try a course of sulphapyridine which proved helpful in a case described by Arnold. It appears to have acted almost specifically on five separate occasions, and the other sulphonamides proved less useful.

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Dr. H. Haber: The focus of the lesion lies within the subcutaneous tissue, which exhibits necrosis of its cells. There are characteristic oil cysts lined by foamy histiocytes which are also found lying between the fat cells. Many histiocytes have also disintegrated, as seen by nuclear debris. There are also several giant cells of the foreign body type and large vacuolated endothelial cells.

A marked inflammatory reaction within the interstitial spaces of the tissue consists of plasma and round cells. The infiltrate continues along the blood-vessels right up to the subepidermal part of the corium. The corium itself shows oedematous separation of its bundles which appear to be sclerosed. There are also many monocytes which exhibit different stages of differentiation to lipophages. The blood-vessels show proliferation, and one vessel lying within the adipose tissue is obliterated. The epidermis shows changes of an eczematous type. The diagnosis is nodular non-suppurative febrile panniculitis (Weber-Christian).

Dr. B. Schwartz: In the case I showed in December (*Proc. R. Soc. Med.*, 1952, **45**, 174) large numbers of the nodules had ulcerated and broken down. Chloramphenicol was used in that case, with quite remarkable results. The lesions healed completely at first and the patient remained reasonably well and ambulant subsequently. A current relapse is again being treated with chloramphenicol. It is probably worth trying here.

Postscript (April).—The patient was given a course of sulphapyridine for five days, which made her extremely ill and produced no improvement. She was then given a course of chloramphenicol: 500 mg. six-hourly for ten days followed by 250 mg. for four days. Rapid improvement coincided with the administration of the antibiotic and all the ulcers, including the large one on the thigh, were practically healed within a fortnight. Her blood count remains unaltered. It is hoped to publish fuller details later.

Acanthosis Nigricans.—Dr. O. L. S. Scott.

Woman, aged 52. She was perfectly well until seven months ago. After a dental extraction and fitting of new plastic dentures she developed gradually increasing

pain and difficulty with eating, noticed a waxy thickening of the palms, and was troubled with persistent lacrimation. She has lost weight, has had vague indigestion, and has noticed the appearance of warty growths, pigmentation and thickening of the skin of the waist and flexures.

Biopsy of the skin from the axilla shows appearances compatible with acanthosis nigricans. Biopsy of one of the enlarged glands in the left supraclavicular fossa shows squamous-cell carcinoma and also numerous melanin-laden phagocytic cells. It is considered most likely that there is a primary bronchogenic carcinoma. No evidence of neoplasm has been found despite careful clinical investigation, barium meal, repeated x-ray of chest, and histamine test-meal.

This case shows involvement of the conjunctiva and buccal mucous membrane and tongue. The main and original symptoms have been pain and difficulty with eating. These have been controlled by mouth-washes before meals with 0·05% percaine in normal saline. This has enabled her to take a high protein, semi-solid diet, which included casein hydrolysate, and massive doses of vitamin A, viz., 150,000 i.u. daily. Her general condition improved greatly. Her tongue showed the greatest change, for when first seen its surface resembled and could be parted like the pile of a carpet. Whether this change in the mucous membrane of the mouth was caused by the treatment it is impossible to say.

Another feature of this case is the presence of the melanin-laden cells in the cervical glands removed for biopsy. I have not been able to find reference to this occurring in other cases of acanthosis nigricans, and the cause is obscure.

The four most plausible theories regarding the origin of acanthosis nigricans are: first, involvement of the abdominal sympathetic nervous system or adrenal glands; secondly, toxaemia from neoplasms giving rise to altered response to light; thirdly, avitaminosis; and fourthly, endocrine disturbance. None of these theories will explain all the cases. H. O. Curth (1948, *Arch. Derm. Syph., Chicago*, **57**, 158), in the most detailed study of the literature so far, including some cases of her own, states that she believes there is no difference between the juvenile so-called benign form and the adult, so-called malignant form of acanthosis nigricans. She postulates a common origin for both, and considers it possible that there is a genetic relation between them and cancer—particularly "gland cancer." She states that the "role of cancer in family histories of patients with acanthosis nigricans, the type of cancers that have been associated with acanthosis nigricans and the chronologic independence of the two conditions are supporting evidence."

Acanthosis Nigricans.—Dr. B. Schwartz.

C. G., aged 45, lorry driver. Attended hospital in February 1952 for removal of the multiple warts on his forearms. These were first noticed in July 1951, and had been increasing in number since. There were no subjective symptoms.

Had been successfully treated for a contact dermatitis in May 1951. The hands and forearms only were affected and the rest of the skin was clear.

30.viii.51: At operation a carcinomatous growth involving the middle and lower thirds of the stomach was found. There were numerous secondaries scattered over the peritoneum, and biopsy of one of these showed omental fat infiltrated with anaplastic adenocarcinoma. In addition there were three metastases in the gall-bladder but none in the liver or any other abdominal viscera. A palliative gastro-enterostomy was performed.

Family history.—Nothing significant.

On examination. There is hyperpigmentation chiefly of the face and neck, the axillae and the groins. On the pigmented areas are numerous warty growths of varying size with a particularly large plaque at the right wrist. The close-set lesions on the hands have given these a velvety appearance.

There are papillary growths around the mouth and extending on to the mucous

membrane and also on the sides of the tongue. There is no excess pigmentation in the mouth.

Blood count normal. B.P. 124/80.

He has gained 4 st. in weight since his abdominal operation and is now completely free from gastric symptoms.

Histology (Dr. H. Haber). -(1) Skin from right axilla shows typical acanthosis nigricans. (2) Skin from right wrist shows verrucose hyperplasia with highly pigmented basal-cell layer.

Comment.—This is, I think, a classical case of acanthosis nigricans.

Two points in this case are worthy of record.

First, because of his previous attendances in the Skin Clinic one can accurately place the time of onset of the skin condition between June and August 1951, i.e., at a time when his abdominal malignancy must have been well advanced.

Secondly, a gastroscopic examination was made by Dr. Avery Jones on 27.ii.52, when the stomach was seen to be rigid and not distensible and the antrum almost completely obstructed. There was no ulceration of the stoma and no evidence of any papilliferous growths.

In the past most of these cases have been associated with a glandular type of carcinoma. It would therefore be interesting to know what the final pathological diagnosis is in Dr. O. L. S. Scott's case.

Kaposi's Multiple Pigmented Haemorrhagic Sarcoma.—Dr. M. Garretts (for Dr. W. N. Goldsmith).

Mr. V. C—, aged 50. Occupation: kitchen porter. Native of Malta.

History.—Four years ago the hands and feet "became black" and swollen, and the feet were painful on walking. The black discoloration gradually faded, leaving the present purplish lesions. The pain in the feet on walking is still present, and there is also some pain in the left ankle. No pain when sitting or lying down. Occasional swelling of left foot and both hands.

Past history.—Syphilis 6 years ago, treated with penicillin for 7 weeks while an in-patient, and arsenic injections for 18 months while an out-patient. Rash 3 years ago. This was extremely irritating and lasted only 7 days. Liver disease many years ago. Winter cough for many years.

Personal history.—No history of trauma. Has been exposed to cold temperatures.

On examination.—Telangiectases over the cheeks and nose. Discrete infiltrated papules and plaques on feet and hands. Colour varies from purple to dark brown. Some are very soft while others are firm. Some pitting oedema on dorsum of left foot. The soles are hyperkeratotic. Just behind the left external malleolus there is a transversely running vein. When the patient is standing this vein can be emptied and seen to fill slowly as if it were impeded. Some nodules can be palpated along the course of the vein.

Cardiovascular system: N.A.D. Blood-pressure 160/100.

Respiratory system: Clubbing of fingers. Few basal crepitations on both sides.

Alimentary tract: N.A.D.

Central nervous system: Pupils equal and react to light and accommodation. Wasting of both lower legs, more on the left. Some blunting of pin-prick sensation over soles and toes. Patient tolerant of tendo Achillis pressure.

Lymphatic system: Tonsils enlarged. Lymph glands—none enlarged.

Investigations.—W.R. and Kahn negative. White cell count 7000 c.mm. Differential: polymorphs 56%, lymphocytes 31%, monocytes 9%, eosinophils 4%.

Sputum—no acid fast bacilli seen.

Liver function tests normal.

Plasma proteins normal.

Cerebrospinal fluid—W.R. negative. Cells and chemistry normal.

Biopsy (15.i.52).—Lesion on medial aspect of right foot. Epidermis shows hyperkeratosis but is otherwise normal. There is a dermal infiltrate most marked in the deeper layers and subcutis. It is composed of vaso-formative tissue and comprises a number of engorged thin-walled vessels. There are also numerous histiocytes, lymphocytes and fibroblasts. In places there are strikingly localized masses of lymphocytes (Marchand's lymphocytoid cells ?), together with a few larger cells with abundant eosinophilic cytoplasm and clear vesicular nuclei. There is some iron pigment around some of the vessels (see iron-stained section). Some of the smaller vessels are obliterated, and there is some hyalinization of the collagen, especially around blood vessels.

Comments. 1. Many workers have considered the early and widespread involvement of the vascular system, with haemorrhages, to suggest a toxic or infectious aetiology. It was decided to try the effect of penicillin treatment on this patient.

There are very few records in the literature of penicillin treatment for this disease. Balina (1949) briefly records one case. The patient was given 4,000,000 units of penicillin. He reports a remarkable result -the skin lesions almost completely disappeared.

Marchionini and Götz (1950) in the *Penicillinbehandlung der Hautkrankheiten* quote Pierini and Grinspan. Two longstanding cases were treated with 4,000,000 units of penicillin. The tumours shrivelled and dried up. After three to five months there was no relapse.

Mr. V. C— was given 300,000 O.u. b.d. of procaine penicillin for eighteen days. Total dosage 10,800,000 O.u. One month later this had produced no change in the lesions. He was then given x-rays to lateral side of left foot—100 kv., 1 mm. Al. filter, 75 r weekly, 3 doses. Two weeks after these three doses no apparent change in the lesions was detected, and there was no relief of the pain, which was the main symptom of the patient.

2. It is interesting to note that this patient came to hospital for pain on walking, especially in the left foot and around the left ankle. The rash did not worry him. The pain was not typical of peripheral arterial disease (not an intermittent claudication type of pain). Dr. E. E. Pochin found his arterial pulses to be normal on oscillometry, and referred him to Dr. Goldsmith.

On close questioning the patient indicated the site of his pain to be localized over dilated veins on the lateral aspects of his ankles. The lesions on the dorsum of the left foot appear to be closely related to the engorged venous channels.

Funk (1889) first noticed the presence of venous ectasia and coiled enlarged veins near the tumours.

Kaposi (1899) described a case with dilated veins on the lower extremities. Many other workers have reported the distribution of nodules of Kaposi's sarcoma along the venous system.

Saphier on post-mortem examination found in one case enlarged and indurated venous stems and nerve trunks.

Conclusions. It is suggested the pain and swelling complained of by the patient were in fact manifestations of the disease.

Perhaps the wasting of his calves and sensory changes are related to nerve involvement.

It would be valuable to learn the experiences of other members who have treated this condition with penicillin or other antibiotics.

There is no evidence recorded in the literature that syphilis is an aetiological factor in this disease.

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Kaposi, M. (1899) *Arch. Derm. Syph Wien*, **49**, 133.
Marchionini and Götz (1950) *Handbuch der Penicillinbehandlung der Hautkrankheiten*, 1950. Berlin: Springer.

Dr. H. T. H. Wilson : I have treated one comparatively mild case with penicillin—300,000 units a day for six weeks without the slightest effect.

Dr. P. Hall-Smith : In a case I described last year I also used penicillin for about ten days, and there was no effect at all. The patient was a woman aged 80. (*Brit. J. Derm.* (1952), **64**, 115).

Kaposi's Idiopathic Multiple Haemorrhagic Sarcoma.—Dr. P. J. Hare.

Mrs. D. S—, aged 58, housewife.

The patient is Jewish ; her parents came from Poland.

She first noticed lesions on the left leg in 1939. Those on the right appeared in 1951. The areas of involvement have gradually enlarged.

On examination there are indefinite, bluish-red, confluent patches on the anterior surfaces of both lower legs. Their surface is smooth, and there is little palpable infiltration. On the right leg there was a hemispherical nodule at the margin of one of the patches, about 0·5 cm. in diameter, brownish-red in colour and rubbery in consistency. This was excised for histological examination. Dr. H. Haber found the microscopical appearances to agree with the clinical diagnosis of Kaposi's sarcoma.

Treatment has not yet been given.

The case is shown because this rare disease is even more exceptional in women. Although the disease has been present for at least 12 years, the skin changes are very slight.

Dr. F. F. Hellier : I had an example in a woman aged about 45, also in an older woman. I have used penicillin without result. I should be much interested to learn whether anybody has tried the effect of ACTH.

Dr. R. H. Seville (following a question by the President) : There are *four* cases attending St. John's Hospital, and three of these are females.

Lichen Striatus.—Dr. R. H. Seville (for Dr. R. M. B. MacKenna).

B. P—, female, aged 51.

Present history.—Six weeks ago the patient suddenly developed a rash on the upper part of her left arm and shoulder which spread rapidly down to within 5 cm. of the wrist. Three weeks ago the rash became more extensive and involved the hair margin of the left side of the face. During the past few days the lesions have started to fade. The rash is sore to touch and does not itch.

Past history.—The patient was perfectly well until one year ago when she developed an itching rash along the anterior hair margin. Within a few weeks the rash had involved the upper part of the back and shoulders ; the affection was bilateral. She was treated for " scurf " by her doctor with good results ; only minor relapses have occurred since. (The patient thought that both facial conditions were similar, except that the present rash is strictly confined to one side.)

Personal history.—For the past six months the patient has complained of flushings and irregular periods.

Family history.—The patient's daughter suffers from seborrhoeic eczema.

Examination.—The affection is seen only on the left side, involving the face, neck, shoulder and arm. The rash is made up of grouped lichenoid and eczematous papules aggregated into linear streaks and bands. One band extends from the chest, narrowing to 1 cm. in width over the biceps, expanding across the left antecubital fossa and continuing along the radial border to within 3 cm. of the wrist. The other extends from the back of the chest and narrows to between 3 cm. and 5 cm. in width on the postero-lateral border of the upper arm. It then becomes less noticeable but can be traced over the posterior surface of the elbow and along the ulnar border to within 7 cm. of the wrist.

General and detailed neurological examination reveals no abnormalities. The rash is not localized to any particular dermatome or area of skin supplied by a cutaneous nerve.

Special investigations.—Skiagram of the cervical spine shows reduction of the disc spaces between the cervical vertebrae 5 to 7, with marginal osteophyte formation especially between the cervical vertebrae 5 and 6. There is no evidence of cervical rib.

Histological section shows two foci of papulo-vesicular eczema (Dr. Haber).

Comment.—This patient is presented because she is clinically similar to Senear and Caro's cases and because I was not able to find another in the Proceedings of the Society.

Postscript.—The patient's rash steadily faded, until at six weeks after presentation only residual pigmentation remained on the flexor surface of her left forearm.

Dr. F. F. Hellier : I saw a case of Dr. C. Stuart's in Leeds about a month ago in which there was a thin narrow line right down the hip to the ankle. It had started on the calf, and the upward extension might have been explained as following some lymphatic spread, but in addition to going up it spread downwards. It was a perfect linear lesion, with emphasis on the calf ; clinically and histologically I thought it was eczematous. I believe the case shown to-day is a similar linear eczema which does not warrant the name of lichen.

Dr. H. Haber : I have seen several cases of linear eczematous eruptions. Histologically they may show different stages of eczema. There may be spongiosis, vesiculation or lichenification. It is possible to think that these cases represent subclinical naevi, which become manifest when they are sensitized.

Dr. J. Overton : I have recently seen a child with a linear, papular lesion on the thigh. The mother stated that she was bathing the child one night when she noticed a small area of papules. Within a few days it had run down the thigh. Three weeks later the lesions had begun to pale and flatten, and a week later they had disappeared completely The duration of the syndrome was about six weeks The lack of symptoms, the character of the lesions and the limited duration with a spontaneous clearance suggests a clear-cut clinical entity Dr. Haber's reference to naevoid origin is very interesting, but how does this fit in with the transitory nature of the eruption ?

Dr. I. Martin-Scott : This case seems to me a mixture of lichen and eczema. I have seen lichen striatus on the arm of a small girl which disappeared spontaneously and showed most of the histological features of lichen planus I have recently had a case of zonal eczema running from the nipple round to the shoulder-blade in a boy of ten years—this is also involuting spontaneously. In to-day's case we have the appearance of lichen planus with the histology of eczema.

Dr. Seville : In 1896 Unna gave an excellent description of this condition which he classified provisionally under "naevi." Similar cases have been reported as linear psoriasis or lichen planus. The classification of lichen striatus lies between naevi and eczema, and I am in agreement with Dr. Hellier in placing it in the eczematous group.

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Unna, P. G. (1896) *Histopathology of the Diseases of the Skin*, translated by Norman Walker. Edinburgh : Clay. P. 1146.

Juvenile Xanthomata.—Dr. C. D. Calnan.

E. F—, girl, aged 6 years.

History.—Small yellow spots were noticed around both eyelids at the age of 8 months, and later on the face, chest, back, arms and thighs.

New lesions appeared at intervals up to the age of 2 years. Since then they have slowly faded and some have cleared entirely without trace, especially under the chin and the front of the neck. Others have left a residual area of pigmentation. Larger lesions have involuted to leave a small loose "bag" of skin.

Some typical xanthoma lesions are still present.

General health unimpaired.

Past history and family history.—*Nil* relevant.

Examination.—There is a profuse eruption, maximal on the abdomen but also on the chest, face and limbs of pigmented macules, and orange-yellow papules up to ½ cm. diam. Some of them show signs of involution.

Liver just palpable, not enlarged.

Spleen and lymph glands normal.

Blood cholesterol 330 mg. per 100 ml. (3.x.47) ; 206 mg. per 100 ml. (8.i.52).

Skiagram of skull : N.A.D.

The following cases also were shown :

Two Cases of Chronic Lymphoedema.—Lieutenant-Colonel K. Greenwood, R.A.M.C.

Cutis Verticis Gyrata.—Dr. Peter Borrie.

Pemphigus Vegetans (Neumann).—Dr. Ian Martin-Scott.

Atrophie Blanche des Jambes.—Dr. C. D. Calnan.

Atrophie Blanche.—Dr. R. H. Meara.

Pityriasis Lichenoides et Varioliformis.—Dr. K. D. Crow.

17 April 1952.

Sclerodermia Dermatomyositis (with Electronmicrographs).—Dr. R. H. Seville.

C. W—, male, aged 56.

History.—The condition started four years ago as a pink rash over the forearm extensors with some swelling; the eyelids were involved three months later, and the skin of the forearms, hands and face became tight and drawn. The patient complained of pain in his elbows and wrists and was given wax baths and gold injections without relief. Three years ago he noticed that he was losing power in his hands, arms and legs, and that his fingers and toes were very susceptible to cold ("dead fingers").

A year later, after recovering from pneumonia, he found he had lost one stone in weight and that he was weak in the shoulder muscles, elbows and upper part of his thighs.

In the past year he has been unable to extend his elbows completely, and has had much pain in his knees, elbows and to a less extent shoulders and wrists. He has also suffered from painful superficial ulcerations of the extensor surfaces of his left knee and elbow. The weakness has been relentlessly progressive and is now his major disability.

He used to drive heavy tankers and his weight was more than thirteen and a half stone. Three and a half years ago he became a storeman, but after two years was unable to continue the work owing to weakness and difficulty in keeping his head erect. His present weight is 8 st. 10 lb. He had not complained of any symptoms suggesting systemic involvement. Apart from suffering from a duodenal ulcer for the past twelve years there is nothing of note in his past or family history.

Examination. The skin of the fingers, hands, forearms and face is tight and drawn: there is a little streaky telangiectasia over the knuckles, and the upper eyelids are slightly purple in colour. Behind the left shoulder is a telangiectatic erythematous and brown area measuring 5 × 3 cm. Superficial ulcerations are present over the left elbow and knee where the skin is tight and erythematous. There is wasting and loss of power in the muscles of the shoulder girdle, the buttocks, the arms, legs, and to a less extent the neck; bilateral contractures are present in the biceps. Several subcutaneous nodules measuring 2 to 6 mm. can be palpated in the tendon insertion on the lateral aspect of the left thigh. General physical examination reveals no abnormalities. Blood pressure 110/70.

Histological section.—(R. forearm extensor). "The epidermis is of basket weave type and acanthosis is present. The collagen in the upper part of the corium is of normal texture, while in the mid-cutis it shows swelling and homogenization of its fibres. Much perivascular infiltration is seen superficially, and a few vessels have

thickened walls and narrowing of the lumina. The elastica appears to be normal in the upper part of the corium and atrophic and even absent within the changed collagen.

"(R. deltoid) Striped muscle shows undulation of its fibres, effacement of striation, increase of nuclei and characteristic lymphorrhages. There is swelling of the walls and interior linings of most of the vessels."—(Dr. Haber.)

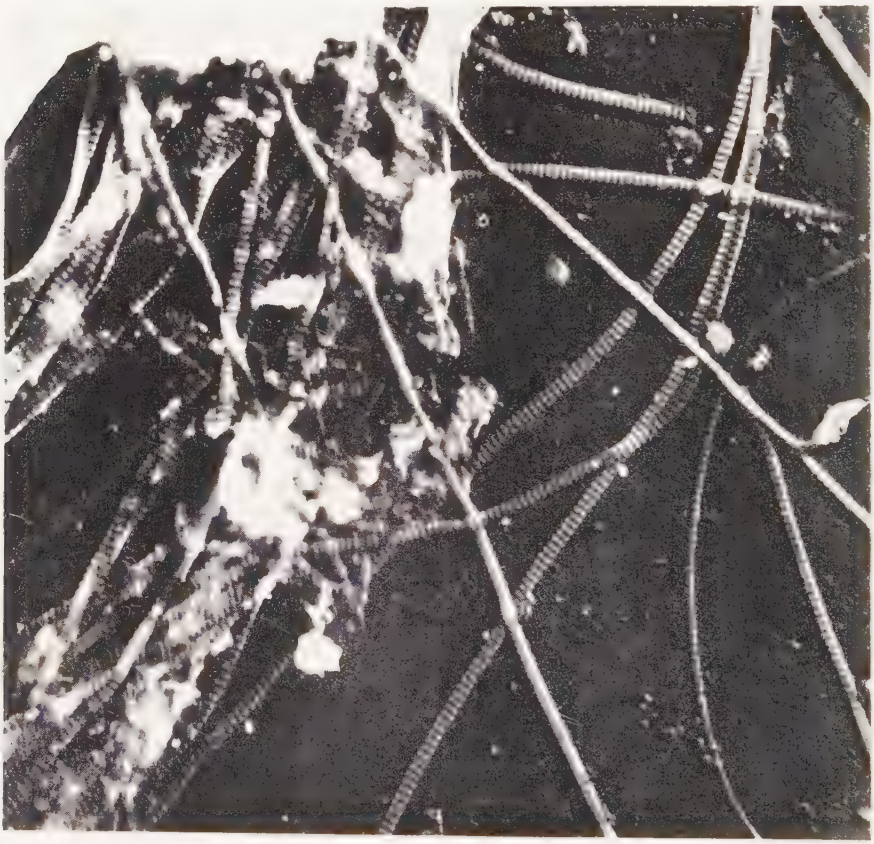

FIG. 1.—Electronmicrograph from sclerodermatous area of skin showing amorphous material and relatively normal fibrils. × 15,000.

Biochemistry.—Creatine excretion (24 hourly):

Before H.P.C., 140 mg. 23 October 1950, 151 mg. 20 June 1951, 54 mg. 21 June 1951; after H.P.C., 220 mg. 15 July 1951, 200 mg. 16 July 1951.

Skiagrams.—Chest: Normal.

Hands and elbows: No atrophy of the terminal phalanges, calcification or osteoporosis are seen; minimal osteoarthritic changes are present.

Wrists, knees and L. thigh: No abnormalities are detected or calcification noted.

Electronmicrographs (from sclerodermatous skin R. forearm). "An increased quantity of amorphous material is present (Figs. 1 and 2), and most of the collagen fibrils are normal. A few fibrils exhibit loss of rigidity and shortening, and very rarely, thinning and fraying of their ends; these changes may be indicative of incipient degeneration."—(Dr. R. Reed.)

Therapy (since 5 October 1950). Testosterone, thyroid, ephedrine, glycine, H.P.C., para-aminobenzoic acid, vitamin E, protein hydrolysate; all without apparent benefit. No change was noted in the histology or electronmicrographs after a course of H.P.C.

Comment. This patient has already been described as a case of intermediate type between scleroderma and dermatomyositis (Dowling, 1952). Electronmicroscopic

Fig. 2.—Electronmicrograph from sclerodermatous area of skin showing amorphous material in clumps and adhering to a fibril. There is minimal bending, shortening and fraying of the ends of the fibrils. × 17,000.

investigation of a sclerodermatous area of skin shows, as far as can be ascertained, exactly the same picture that is encountered in scleroderma. This agrees with Dr. Dowling's views as to the identity of dermatomyositis and scleroderma.

The electronmicroscopic examinations were made by Dr. Reed, and we hope to give an account of the methods used in a subsequent publication. In scleroderma, the main change is a great increase in amorphous material seen in the electronmicrographs. The quantity of this material seems to be proportionate to the degree of swelling and homogenization seen in histological section. Trypsin or ether will remove the amorphous material, leaving collagen fibrils which are practically all of normal width.

The general difficulties in electronmicroscopy have already been stressed last month at the meeting of the Section of Pathology. Bearing these in mind, we suggest that the amorphous material is in effect ground substance and this is primarily changed in sclerodermia. Dr. Musso and I are at present working on the subject using histological techniques at the Institute of Dermatology.

REFERENCE.

DOWLING, G. B. (1952) *Proc. roy. Soc. Med.*, Section of General Medicine one month previous to this meeting.

Acknowledgment is made to Professor W. T. Astbury of the Department of Biomolecular Structure, Leeds University, for the electronmicrographs.

Dr. J. OVERTON: How early do these changes take place in this disorder and are they reversible?

Dr. L. FORMAN: Have the collagen bundles ever been observed to undergo gross alteration when examined with the electron microscope? It is a fact that eventually in sclerodermia the collagen bundles do disappear and are replaced by new scar tissue.

Dr. SEVILLE (in reply to Dr. Overton and Dr. Forman): I cannot answer the questions from the electronmicroscopic aspect as we have examined neither an early case where histologically the fibres appear swollen nor one where resolution has taken place. I have done a biopsy on an area of skin which a patient stated was sclerodermatous twenty years previously. Clinically there were exposure changes as the patient had spent most of her life in India. Histologically "senile elastosis" was seen and the pilosebaceous apparatus had disappeared leaving the arrectores pilorum muscles intact; apart from these changes the collagen bundles looked normal.

The following cases also were shown:

Dermatofibrosarcoma Protuberans. Dr. A. PORTER and Dr. H. HABER.

Cutis Verticis Gyrata.—Dr. J. G. HOLMES (for Dr. G. B. MITCHELL-HEGGS).

Lupus Vulgaris, Untreated for Over 30 Years.—Dr. N. A. THORNE (for Dr. W. J. O'DONOVAN).

NORTH OF ENGLAND DERMATOLOGICAL SOCIETY.

Manchester, May 1952.

Arteriovenous Fistula.—Dr. B. P. Mumford.

N. D—, a boy, aged 13.

History.—Three years ago an ulcer appeared in the first interdigital cleft of the right foot, which was at times extremely tender and painful with little sign of healing. Local applications had no effect, but some improvement occurred after the application of occlusive dressings. The patient complained of occasional swelling of the right ankle and foot. Neither the patient nor his parents had noticed any discrepancy in the size of the affected limb compared with the left.

Previous history and family history.—*Nil* relevant.

On examination.—An ulcer with a red granulomatous base is present between the 1st and 2nd toes of the right foot, and the surrounding skin shows a purplish discoloration. The affected leg is darker in colour and warmer. There is a capillary angioma present on the right side of the face. Varicose veins are not present.

Investigations.—Measurements: Length—the right leg is 5·0 cm. longer than the left, measuring from the anterior superior iliac spine to the medial malleolus.

Venous pressure: R. leg 82 mm.; L. leg 62 mm.

Oscillation pressure: R. leg 14; L. leg 10.

Oxygen saturation of venous blood in R. leg 90%.

Skiagram of chest showed enlargement of the heart but no abnormality in lung fields.

Arteriogram of the right leg did not visualize a fistula, but showed considerable filling of small arteries in the distal part of the foot and in a small area around the knee.

Filling time to the tip of the toes on the right leg was 4 seconds (normal 17 seconds).

Comment.—Small arteriovenous fistulae may close spontaneously, while continuous pressure by means of bandages may encourage thrombosis, but the results are not predictable. Attempts to alleviate the condition by surgical intervention may be difficult owing to the diffuse nature of the condition and the number of fistulae present, though Wright (1948) states that it should be attempted to prevent the development of the following complications: (1) Cardiac enlargement with cardiac insufficiency due to the size of the shunt; (2) venous insufficiency with the risk of ulceration or gangrene; (3) enlargement of the limb if the epiphyses have not closed.

Sympathectomy has been known to give temporary relief, but some cases require amputation. Others have been known to survive to adult life without apparent complications.

Reference.

Wright (1948) *Vascular Disease in Clinical Practice.* Chicago: The Year Book Publishers.

Acrokeratosis Verruciformis (Hopf).—Dr. P. B. Mumford.

An Irishman, aged 32.

History.—The lesions began on the backs of the hands 14 years ago, later appearing on the upper part of the chest, neck, arms and knees. During the last 4 years the condition has remained unchanged.

Family history.—There is no family history of a similar condition and no parental consanguinity.

On examination.—On the backs of the hands, fingers and knees the tumours are slightly raised with mildly verrucose surface resembling large plane warts. They are very numerous, and many show a tendency to confluence. On the chest and neck the

lesions show varying degrees of pigmentation similar to that seen in seborrhoeic warts.

Histology (Dr. J. G. Coburn).—The epidermis shows moderate acanthosis with many vacuolated cells in the upper part of the rete. The granular layer is well preserved, while the overlying keratin, though laminated, does not show the typical "basket weave" appearance of epidermodysplasia verruciformis.

Comment.—It seems likely that this condition is closely allied to the epidermodysplasia verruciformis of Lewandowsky and Lutz, varying only in its distribution and to some degree in the histology of the individual lesions. Lutz has now concluded that the dermatosis is a generalized eruption of verrucae planae, assuming its particular aspect in accordance with the soil on which it develops. The histological picture is also similar to the condition described by Unna as the hard naevus.

Two Cases of Trichophyton Sulfureum Infection.—Dr. J. Curry.

C. H—, a boy, aged 3; R. W—, a boy, aged 5.

History.—The children live in adjacent houses. The elder boy has had the infection for at least 22 months and the younger boy for 8 months.

In both cases the first lesion was a slightly reddened discoid area of partial baldness on the scalp with a few broken hairs. In the older boy, 9 months after the onset, multiple patches resembling tinea circinata appeared on the face and neck, and subsequently a similar lesion on the left forearm. In the younger boy the infection remained confined to the scalp.

Family history.—No other member of either family was infected and no common source of infection was found.

Investigations.—Wood's light showed no green fluorescence in either case, but in C. H— certain hairs had a dead white appearance.

Microscopy was inconclusive in R. W —, and difficulty was experienced in obtaining a sufficient number of diseased hairs for adequate examination.

Culture: Difficulties were experienced in the case of R. W—, but repeated cultures eventually yielded a pure growth of *Trichophyton sulfureum*. A similar growth was obtained from C. H— at the first attempt.

Treatment.—Both cases were uninfluenced by a variety of local fungicides. It is intended to epilate both cases.

Comment.—The striking feature of case R. W— was the long interval between clinical diagnosis and laboratory confirmation. *T. sulfureum* is a variant of the crateriform group which occurs in follicular tinea capitis, kerion tinea corporis (inflammatory type) and rarely in tinea pedis.

Twenty other cases were shown.

NORTH BRITISH DERMATOLOGICAL SOCIETY.

Glasgow, 13 March 1952.

Foreign Body Granuloma of Face.—Dr. R. W. Carslaw.

Mrs. J. M—, aged 40.

The patient was first seen on 18.v.51, when she complained of a raised nodule in the site of scarring which had been caused by a motor accident 35 years previously. The nodule had been present for three months.

During the next six months the condition regressed and only a small indurated area on the upper lip remained. This was excised by a plastic surgeon, and on examination in March 1951, all that remained was a bright red telangiectatic patch on the right cheek and in the centre of the upper lip some brownish staining and fullness of the red margin.

Investigations.—Skiagram of chest normal.

Histology.—This proves to be an old-standing silica foreign body granuloma. The giant cells contain crystals or amorphous masses of foreign material, some of which is anisotropic when examined by the polarizing microscope. The non-anisotropic masses are probably covered by opaque organic material and this is confirmed by the fuchsinophil staining of some of the crystals, which would not be coloured unless covered by a stainable material.

Severe Psoriasis Treated with AT 10 and Eucortone. Dr. M. S. Smith.

A man, aged 39.

History.—The patient has had recurrent attacks of psoriasis during the past thirty-two years. The present attack is of over a year's duration.

On examination (before treatment). Extensive plaques of psoriasis are present on the trunk. The eruption is confluent over the limbs and the scalp is involved.

Treatment and progress.—AT 10, 10 minims *t.i.d.* and eucortone 1 ml. twice weekly started September 1951. Vaseline locally.

After the third week of treatment the lesions had become paler. Complaint was made of pain in knee-joints and lower limbs. After two months' treatment the lesions were noted to be fading steadily, and rapid fading of the lesions took place after ten weeks of treatment. Administration of AT 10 was discontinued after three months' treatment. The eruption had then disappeared almost completely, and only staining and slight scaling over the hips, sacrum and legs remained. Eucortone was discontinued after a further nine injections, and when the patient was seen five months after treatment was commenced the skin was clear.

The serum calcium remained normal during treatment.

The glucose tolerance test was normal before treatment and six months after treatment.

Lupus Erythematosus Treated with Mepacrine. Dr. F. D. Cohn (for Dr. M. S. Smith).

A woman, aged 45.

History.—Lupus erythematosus appeared on the face eight years ago, and on the fingers eighteen months ago. The patient has attended at intervals over the past eight years and on two occasions became well after a course of bismuth injections. The present eruption on the face began severely a year ago.

Past history.—No previous illness.

On examination (July 1951).—Many small lesions are present over the whole face and, for the first time, on the fingers.

Investigations.—No evidence of focal sepsis.

Treatment and progress.—Course of Lertigon injections given with quite a marked improvement in July 1951. The lesions were again very active in January 1952. Mepacrine 0·1 g. *b.i.d.* commenced. When next seen three weeks later heat and itching were much less and the skin was faintly yellow. The patient complained of constipation. The facial lesions continued to fade, and by the fifth week of treatment they were almost imperceptible. At this time the lesions on the fingers had improved but were still present. After six to seven weeks' treatment, mepacrine was discontinued. To-day faint pigmentation is present over the previously affected areas, and the finger lesions have faded considerably in the past nine days. The yellow discoloration has at no time been very obvious.

The following cases also were shown :

Dr. J. Sommerville : **Blue Naevus ; Bowen's Disease.**

Dr. R. W. Carslaw : **Rosacea-like Tuberculide ; Lupus Vulgaris of Oral Mucous Membrane.**

Dr. F. D. Cohn: **? Reticulum-Cell Sarcoma; ? Histiocytoma; Mycosis Fungoides (2).**

Dr. F. D. Cohn (for Dr. M. S. Smith).—**Lupus Erythematosus under Mepacrine Therapy (3).**

Dr. M. S. Smith: **Atypical Erythema Nodosum.**

SOUTH-WEST OF ENGLAND AND WALES DERMATOLOGICAL SOCIETY.

Bristol, 16 February 1952.

Tinea Capitis (Trichophyton violaceum).—Dr. M. Hewitt (for Dr. R. P. Warin).

P. N—, a schoolgirl, aged 7.

History.—In December 1947, when the patient was 2 years of age, her mother noticed a scaly patch of alopecia on her crown. A diagnosis of seborrhoea capitis was made, and she attended a hospital regularly until March 1949. During the period considerable scaling was constantly noted but no broken hairs were described. The condition did not improve, and the scaly areas in the scalp persisted until the child was seen in July 1951. Examination then revealed scattered scaly patches in which the hair was slightly thinned and individual hairs could be easily and painlessly plucked. There was no fluorescence on exposure to Wood's light. Microscopically, a hair from the affected area was found to be packed with spores.

Samples were sent to the Mycological Reference Laboratory of the London School of Hygiene and Tropical Medicine in November 1951. Dr. J. Walker reported that hairs taken from the left side of the vertex yielded 10 colonies of *Trichophyton violaceum* and one of *T. discoides*. Those from the vertex yielded *T. violaceum* only.

Treatment was started in July 1951 by twice daily application of acid. benzoic. 3 parts, acid. salicylic. 3 parts, ung. emulsificans aquosum 94 parts, and bi-weekly shampoos with 1% cetrimide.

Salicylanilide ointment was substituted for the above ointment for a period of 3 weeks in December 1951: Salicylanilide (I.C.I.) 4·5 parts, cetrimide 1 part, distilled water 4 parts, carbowax 1500 90·5 parts.

Later results of cultural examination of hairs: January 1952, three specimens—negative: February 1952, four specimens—negative: April 1952, two specimens—negative.

Comment.—There was no relevant family history and no known contact either here or from abroad. It seems reasonable to assume that this is a *T. violaceum* infection of at least 5 years' duration with relatively scanty clinical signs. It is difficult to assert a double infection on the grounds of one reported colony of *T. discoides*. This had been the only known *T. violaceum* infection in Bristol until 11 February 1952, when a further case was identified. The patients lived several miles apart, attended different schools, and again in this new case the source of infection is unknown.

Reticulosarcoma Simulating Tertiary Syphiloderm.—Dr. E. Prettejohn (for Dr. C. D. Evans).

F. B—, a man, aged 67.

History. The patient was first seen in July 1951. Eight months previously a number of nodules had appeared on the left leg and lower thigh. One month previously the largest of these lesions on the outer side of his left knee had ulcerated.

On examination (July 1951). There were brownish-pink nodules situated mainly on

the front of the left shin and thigh, many arranged in a circinate pattern. There was a large lesion on the outer side of the knee, in the centre of which was an ulcer about 4 × 3 inches.

A diagnosis of tertiary syphiloderm with ulceration was made, but the Wassermann and Kahn reactions were both negative. A full blood count showed no abnormality.

Treatment with iodides, 4 injections of 0·2 g. bismuth, 12 mega units of penicillin, was given without effect.

In view of this a biopsy was performed and reported on as follows (Dr. A. L. Taylor): "Histologically the nodule is seen to be made up of an infiltration of the whole thickness of the dermis by round, or sometimes polyhedral, cells lying in a delicate network of reticulum. The cells have round or oval nuclei, lightly staining for the most part, but hyperchromatic nuclei are quite frequent and mitoses numerous. The appearances are those of reticulosarcoma."

X-ray therapy was started (total dosage 1430 r to each area at 220 kV: 13 treatments in 34 days). The result has so far been satisfactory. The large ulcer is healing, and the other smaller nodules have disappeared.

Dermatomyositis Treated with H.P.C. and A.C.T.H. Dr. C. D. Evans.

E. A. H—, a woman boxmaker, aged 55.

History.—The patient had been in good health until October 1951, when she noticed stiffness and weakness of the arms and legs. The weakness progressed and she was soon unable to rise from a kneeling position. Two weeks after the onset of the illness a red irritating rash appeared on the hands, face, limbs and trunk. The lower eyelids became swollen.

On examination (December 1951). There was marked generalized muscle weakness. A streaky erythema was present on the face, neck and extremities. Slight puffiness of the lower eyelids was present, and longitudinal haemorrhages could be seen at the bases of the finger-nails. The scalp hair was thinned, particularly in the frontal region, where most of the hairs were broken off with the exception of a fringe of hair at the hair margin. There was a low pyrexia.

Investigations.—Blood: Hb 95%. W.B.C. 10,500, polys. 55·5%, lymphos. 17, monos. 10, eos. 17·5%.

Urinary creatine (19.xii.51) 0·66 g. in 24 hours. (22.ii.52) 0·408 g. in 24 hours.

Skiagram of chest: normal.

E.C.G.: Left axis deviation with small P waves.

Histology.—Muscle: Scattered patches which show poor staining and loss of striation; lymphocytic infiltration between the fibres.

Skin: Slight hyperkeratosis and acanthosis. The papillary processes are flattened. In the dermis mononuclear cell infiltration, particularly around small blood vessels. Numerous eosinophils. With crossed prisms the collagen fibres can be seen to be disintegrated.

A biopsy taken after H.P.C. treatment showed that the collagen was still disintegrated but the majority of the fibres were lying horizontally.

Treatment and course.—3 hydroxy-2-phenylcinchoninic acid (H.P.C.) 500 mg. twice daily for 15 days produced no change in the clinical condition. On 22.ii.52 a course of A.C.T.H. was started. A total of 1·75 g. was given in 19 days without clinical improvement. The eosinophil count fell from 500 c.mm. to 10 on the first day and remained at this figure.

Comment.—In view of the association of dermatomyositis with malignant disease (Forman, 1952) a constant watch was kept for evidence of such disease; so far nothing has been found.

A point of considerable interest was the curious frontal alopecia with the fringe at the hair margin. An identical condition has been seen in two cases of acute dissemi-

nated lupus erythematosus and one case of subacute lupus erythematosus which later developed scleroderma. This condition appeared before the administration of A.C.T.H.

REFERENCE.

FORMAN, L. (1952) *Brit. J. Derm.*, **64**, 65.

Ulcerative Colitis with Pyodermia.—Dr. R. P. WARIN.

B. L—, a railway signalman, aged 50.

History.—The patient has complained of abdominal discomfort after meals since 1942. In November 1950 he developed diarrhoea with blood in the stools and at the same time was noticed to have acneiform lesions over the upper part of the back. These included pustules and comedones. Some of the lesions were granulomatous and one on the nose had an appearance suggesting epithelioma. No medicines containing iodides or bromides had been taken.

The diarrhoea and acneiform lesions continued, and in March 1951, coinciding with an exacerbation of the diarrhoea, ulcers developed over the arms, trunk and legs. About ten ulcers were present, some being about 10 cm. diameter with deep sloughing bases and raised creeping edges. At this time he was admitted to hospital, and after three weeks the diarrhoea improved after a course of phthalylsulphathiazole 1·0 g. *q.d.s.* Coincident with this improvement the ulcers began to heal and 3 or 4 weeks later had all healed.

He was discharged from hospital, and except for the acneiform lesions and 2–3 loose stools a day he remained well until October 1951. He then had a relapse of the colitis and again developed large ulcers on the trunk and limbs. He was again admitted to hospital but failed to improve on various treatments, including a further course of phthalylsulphathiazole. After 4 or 5 weeks the diarrhoea began to improve, and again coinciding with this the ulcers began to heal. After a further 4 or 5 weeks the latter were healed and he was discharged.

Since then he has had slight diarrhoea but no major exacerbations. The ulcers have remained healed, but a few follicular pustules occur from time to time over the back.

Past history.—He had a little acne vulgaris as a youth, and some scars are present over the shoulders suggesting old acne lesions.

Family history.—Youngest of 21 children. No similar condition in the family.

Investigations.—Sigmoidoscopy: Typical appearances of ulcerative colitis. Fractional test meal and barium meal: Normal. Blood: Secondary anaemia which has fluctuated with the severity of the diarrhoea and loss of blood in the stools. Sternal marrow: Normal. Blood Wassermann and Kahn reactions: Negative. Swab cultures from ulcers showed various bacteria, including a coagulase negative micrococcus and a coagulase positive staphylococcus. Stools: Blood and pus present. No amoebae present. Urinary 17-ketosteroids in 24 hours: 7·6 mg.

Comment.—The interesting features shown by this case of ulcerative colitis are: (1) Initially the lesions were acneiform, including comedo formation. (2) The ulceration fluctuated within a few days with the onset and offset of the exacerbations of diarrhoea. (3) The ulceration was widespread, involving arms, legs and trunk.

BOOK REVIEWS.

A French Dictionary.*

In the preface of this new dictionary the author claims the fact of its existence as its chief merit. He is far too modest, for this well planned, clearly printed and strongly bound volume will provide translators with a much-needed tool. To compress into a single volume of convenient size the unwieldy vocabulary of the medical and biological sciences is a formidable undertaking, and it is surprising how many of the less familiar terms Dr. Lépine has been able to include. As a result of this refusal to confine the dictionary to the commonplace and utilitarian there are few pages not enlivened by the exotic or unexpected word. It is a pleasure for example to learn that *Fletcherisme* is " the thorough mastication of food."

Despite the wide scope of this dictionary and its relatively small size few omissions of important words in current use in general medicine could be detected. Dermatology however, has fared rather less well. The British dermatologist seeking enlightenment on such common and confusing terms as *eczématide, dermatites polymorphes* and *érythème polymorphe* will search in vain.

Gibert is rightly included, as his eponymous association with pityriasis rosea is still common usage in France. Duhring, Fordyce and Darier are all present, but Brooke's disease is given as a synonym for Darier's disease. Pringle, Sjögren, Hailey and Hailey, Senear and Usher and other familiar companions of the English-speaking dermatologist are absent, and Gougerot's name is linked only with a pluriglandular syndrome.

The French definitions of English terms are clear, concise and accurate. The English definitions often fail to achieve as high a standard, and are sometimes clumsily worded and occasionally misleading. *Acanthose* is defined as " any disease of the prickle layer of the skin," and *acantholyse* as " atrophy of the prickle layer of the skin " both questionable definitions. In the English-French section of the dictionary, however, acanthosis is correctly defined as " *Lésion cutanée caractérisée par l'épaississement du corps muqueux de Malpighi*," and acantholysis as " *état particulier des cellules du corps muqueux de Malpighi characterisée par la diminution de leur adhérence réciproque*." It is refreshing to find *prurit vulvaire* translated " pudendagra pruriens," its ponderous syllables evoking memories of Willan and Bateman, but the more conventional term should not have been omitted. " *Spinocellulaire* " is more commonly employed than " *Malpighien* " for squamous-cell carcinoma.

Such omissions and errors are inevitable in the first edition of a dictionary such as this. It is surprising that there are so few. The dermatologist, however wide his reading, will find in this useful dictionary the vast majority of the words he is likely to encounter, and will derive pleasure from the chance discovery of words whose very existence he had never suspected. A. J. R.

Acne and the Endocrines.†

The original work of this thesis is on the hormonal excretion in acne vulgaris. A part of it which was done in association with Professor Quiroga, who has contributed a preface to this book, was published earlier and reviewed in this Journal

* *Dictionnaire Français-Anglais, Anglais-Français des Termes Médicaux et Biologiques.* By Pierre Lépine. London: H. K. Lewis & Co., Ltd., 1952. Pp. 829. 63*s.* net.

† *Acne juvenil polymorfo.* By Rodolfo Nestor Corti. Buenos Aires: El Ateneo, 1952.

(1952, **64**, 74). The excretion of 17-ketosteroids was estimated in a series of normal men and women and in those with acne vulgaris. In the latter series the amount was raised. Of 10 patients with papulo-pustular acne who were given oestradiol benzoate, 8 improved. The author emphasizes that correction of hormonal imbalance is only one part of the treatment, and his book is a good review of the whole aspect of this disorder. G. W. B.

Tropical Dermatology.*

A good physician in the tropics would be a good physician anywhere, for in any region where he might be the affections peculiar to his area would form only a part of the ills that afflict mankind generally. The same may be said of dermatology. In many parts of the world the scattering of dermatologists is very thin, so one may assume that a book on tropical dermatology is intended mainly for the general practitioner in those regions. So far as the reviewer knows, this two-volume work, the first half of which is now to hand, is the only comprehensive book of its kind.

The editor opens with a general survey which, *inter alia*, will be helpful to those who may be confused by the prevalent overlapping of nomenclature. This is followed by sections on skin diseases due to protozoa, spirochaetes and related conditions, affections due to bacteria and cocci, rickettsia and virus infections. The final chapters of this volume are on the miliaria group of dermatoses and on tropical acne. What is missing will presumably appear in the second volume. The editor has enlisted 80 contributors, and as in any platoon of recruits one or another occasionally gets out of step, so here where there is overlapping there is not necessarily agreement. The article on desert sore stresses its rarity in the indigenous population and its higher incidence in poor pigmenters; it is referred to as a diphtheritic infection in the differential diagnosis of tropical ulcer, but it is not regarded as an infection due to *Corynebacterium diphtheriae* in the article on cutaneous diphtheria, which itself gives a meagre clinical description of the cutaneous manifestations of that infection.

From the point of view of the lone practitioner in the tropics who has no special dermatological knowledge more practical details of simple treatment would add to the value of the book. It is unlikely that he will be able to improve his furunculosis patients with general ultra-violet ray baths, and an air-conditioning unit is even less likely to be available for many of his prickly heat clientele. The problem of secondary pyogenic infection in prickly heat is hardly even mentioned in the article on the miliaria group of dermatoses.

Despite these criticisms this volume will nevertheless interest and be useful both to specialists and to those general practitioners who have to do some tropical dermatology. The numerous illustrations are uniformly very good and each section has references to the literature. The book is well printed, and the binding looks stout enough to withstand tropical usage. G. W. B.

Carcinoma and Precancerosis of Male Genitals.†

In some countries of the Far East carcinoma of the penis is not so uncommon, but in Japan the author, despite an interest in the problem for more than thirty years, has seen only about 200 examples. They included about 60 of the proliferative type

* *Handbook of Tropical Dermatology and Medical Mycology.* Vol. I. By R. D. G. Ph. Simons. Amsterdam: Elsevier Publishing Co., Distributors: Clever-Hume Press, London, 1952. Pp. 845. Illus. 587. Price £10 for 2 volumes. Separate volumes not available.

† *Carcinoma and Precancerosis of Male Genitals.* By Shin-Ichi Matsumoto. (1951.) *Monographiae Actorum Dermatologicorum*, No. 12. Instit. Dermatosyphil., Kyoto University, Japan.

with extensive and early destruction of the glans and prepuce, which made it almost impossible to determine whether there had been an antecedent pre-carcinomatosis, but even in some of these and in most of the others he found clinical and histological evidence of precarcinomatosis and inflammatory changes. Giant cells, particularly those of foreign body type were noted in 10% of carcinomas and in some examples of precarcinomatosis.

The usual sites of carcinoma and precarcinomatous conditions were the glans and inner surface of the prepuce of a penis that was or had been phimotic, but not necessarily in a severe degree. Leucokeratosis, cornu cutaneum, erythroplasia and papillomatosis were the commonest precarcinomatoses. Paget's and Bowen's diseases were seldom seen, and then only in rudimentary atypical forms.

A not infrequent finding was the association with leucoplakia of the suggestion of developmental anomalies (apart from phimosis), of adhesions, hypoplasia of the glans and congenital stricture of the urethral orifice.

Interesting sidelights on the prevalence of some dermatological affections in Japan occur here and there in the text. "Epidermodysplasia verruciformis, which is, like xeroderma pigmentosum, rather frequently to be found in this country." "The author in his clinic was able to collect only several cases of leucoplakia of the mucous membrane of the mouth during a period covering more than a quarter of a century." "Lichen ruber and psoriasis vulgaris, extremely and relatively rare diseases respectively in this country."

This painstaking monograph, fully documented and illustrated, is written in clear English and is an authoritative account of the subject. G. W. B.

Diseases of the Scalp.*

The book was written to present a study of the scalp, covering all aspects of its embryology, anatomy, physiology, pathology and treatment. This has been achieved very successfully, and the result is a work which will be used as the standard textbook of reference on the scalp. The text is full of interest. It is intriguing to read that the point to look for in differentiating between man and the ape is that the latter does not part his hair. Hair does not turn white in a night—pigmented hair-shafts are shed and replaced by non-pigmented shafts.

Professor Astbury's work on hair and yarn is given full prominence in the section on permanent waving.

Concerning percutaneous absorption and permeability, a point of considerable interest mentioned is that in animals the sweat glands open into the hair follicles above the sebaceous gland ducts—an explanation, therefore, of why animals do not suffer from prickly heat.

Lard and vitamin F, the active isomer of linoleic acid, penetrate the intact stratum corneum to a deeper level than any other substance. Even so, a depth of only one-third of the stratum corneum is reached.

The section on the endocrines is particularly well presented. The work of the majority of authorities is offered in an unbiased way, allowing full appraisal of the theories and conclusions.

To make "hard" water soft for shampooing, add 1% sodium hexametaphosphate—a useful point in Chapter 2, which deals in a meticulous manner with the astronomical subject of the hair preparations, applications, etc. Apparently there would be no further cases of paraphenylenediamine dermatitis if sufficient oxidizer were added to the preparation, the cause of the dermatitis being the incomplete oxidation of the unstable quinone diimine.

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* *The Scalp in Health and Disease.* By Howard T. Behrman, A.B., M.D. London: Henry Kimpton, 1952. Pp. 566. 312 illus. Price 95*s*.

The section on fungus infections of the scalp draws attention to a very important point not widely known to school medical officers, viz., that Wood's light is not the be-all and end-all of diagnosis in this condition: in other words, certain forms of tinea of the scalp do not fluoresce under Wood's light. This good advice is somewhat vitiated by the neglect to include it in the proforma to School Boards, in which the use of Wood's light in prevention is recommended.

In the final chapter on new growths, 35% of cases of carcinoma of the breast and 20% of all other carcinomas are stated to produce tumours of the scalp. The scalp tumour may be the first sign of metastatic carcinoma before the primary growth has become manifest.

The printing and illustrations are excellent, and the tables of references are exhaustive.

If there is any criticism to make (passing over the reference to the Royal Infirmary of Scotland) it is that the book is *too* comprehensive—with little expansion it would become a complete textbook of Dermatology. A. B.

CURRENT LITERATURE.

PANTHENOL: ITS TOPICAL USE IN CUTANEOUS ULCERATION. F. C. Combes and R. Zackermann. (1951) *J. invest. Derm.*, **16**, 379.

A well known rats' hair-restorer is used as a dressing in 51 heterogeneous cases of cutaneous ulceration. "It is likely that with the use of auxiliary and supportive therapy (such as could be included in actual treatment but not in the present *clinical investigation**), particularly in crural ulcers, Panthenol will produce even better results than in this study."

J. H. T. D.

THE GAMMA GLOBULINS IN SOME DISEASES OF THE SKIN. T. Cornbleet and J. de la Huerga. (1951) *J. invest. Derm.*, **16**, 401.

The turbidometric method of de la Huerga and Popper for assaying gamma-globulin is here recommended as within the capacity of the average laboratory technician, and accurate in so far as the results conform "to a surprising degree" with those of the cumbersome difficult and time-consuming standard method of electrophoresis. Values recorded in this study ranged between 1·01 and 3·24: anything above 1·25 is considered "abnormally high."

J. H. T. D.

WATER EXTRACTABLE CONSTITUENTS OF HAIR. A. Bolliger. (1951) *J. invest. Derm.*, **17**, 79.

Extraction by hot water of 100 g. clipped rabbit-fur yields, with no visible alteration of the appearance of the hair, 3·5 g. of protein-free solid. This consists of uric acid, glycogen, pentose, amino-acids, etc., and is considered to represent by-products of the change from epidermal protoplasm to keratin.

Human hair and sheep's wool seem to be very poor in these substances; for example 7–12 mg.% of uric acid in human hair and 20 mg. % in sheeps' wool as compared with 400 mg. % in the rabbit, phenol 28 mg. % in man and 300 mg. % in the kangaroo. The rabbit has no sweat glands, neither has the dog; rabbit fur yields 500 mg. % of glycogen, dog hair none at all.

The reviewer has no experience of kangaroos, but he has observed that people and dogs have shampoos and that sheep get left out in the rain. On the other hand it is not very clear why, in view of the ease of extraction, there should not be greater variation between individuals of the same species.

Another factor is of course that the hair of man, sheep and poodles goes on growing till it is cut, while that of short-coated animals must be continually replaced. There are dogs that moult regularly and, to judge from the existence in these hard times of dogs' beauty parlours, there must also be dogs that moult irregularly. It seems to the reviewer that the residual water-extractable constituents of hair or fur must depend more on these adventitious factors than on specific variations in metabolism.

J. H. T. D.

THE TREATMENT OF LEPROSY WITH CONTEBEN. Ernest Keil. (1951) *Internat. J. Leprosy*, **19**, 437.

Although more expensive than the sulphone preparations, conteben, a thiosemicarbazone, was better tolerated and appeared to act more rapidly. The initial dose of 25 to 50 mg. was raised to a maximum of 150 mg. daily.

H. T. H. W.

STUDIES ON SERUM PROTEINS IN LEPROSY: THE ALPHA, BETA AND GAMMA GLOBULIN FRACTIONS. Sister H. Ross and F. Gemar. (1951) *Internat. J. Leprosy*, **19**, 445.

Elevation of serum globulin was common in advanced lepromatous cases. Although results were variable, the gamma globulin was more frequently raised than the alpha and beta fractions. There was no definite correlation between gamma globulin increase and thymol turbidity readings.

H. T. H. W.

* Reviewer's italics!

EFFECT OF ADRENOCORTICOTROPIC HORMONE AND CORTISONE ON THE SEVERAL VARIETIES OF PEMPHIGUS. C. N. Frazier, W. F. Lever, R. W. Leeper, C. S. Keuper, L. J. Bienvenu, J. E. Le Donne and S. W. Levy. (1951) *J. invest. Derm.*, **17**, 55.

Between April, 1950, and January, 1951, 2 cases of pemphigus vulgaris, 2 of pemphigus foliaceus, 1 of pemphigus vegetans and 3 of the "acute malignant form of pemphigus vulgaris" were treated with A.C.T.H. or cortisone. All improved, but in some cases a daily dose of as much as 300 mg. (A.C.T.H.) was needed. This account gives the impression that life can be prolonged indefinitely. The ages of the patients are not given, but the one portrayed looks younger than we are accustomed to see in pemphigus. J. H. T. D.

GENERALIZED ERYTHRODERMIA OCCURRING IN A CASE OF PSORIASIS ON TREATMENT WITH ADRENOCORTICOTROPIC HORMONE. D. Cohen and I. H. Distelheim. (1951) *J. invest. Derm.*, **17**, 61.

The diagnosis of such a well-known condition as psoriasis could surely be taken for granted without elaborate verbal description, at least where a good clinical photograph is provided. Indeed the verbal description quite spoils even if it doesn't flatly contradict the effect of the picture. For example, ". . . multiple cyclic papular lesions over the entire integument . . . merged to form coalescent patches . . . micaceous scales . . . scales somewhat branny in consistency . . ." But doesn't psoriasis vulgaris occasionally "eventuate" into a generalized (*sic*) erythrodermia without any treatment at all? J. H. T. D.

IRON, COPPER AND ASH CONTENT OF HUMAN HAIR OF DIFFERENT COLOURS. T. F. Dutcher and S. Rothman. (1951) *J. invest. Derm.*, **17**, 65.

Not only does the pigment of red hair contain iron, but the total iron content of the hair is about 5 times that of hair of other colours. The amount of copper doesn't vary.

J. H. T. D.

A COMPARISON OF THE DIRECT ACTION OF ESTROGEN AND ADRENAL CORTICAL EXTRACTS ON GROWTH OF HAIR IN THE RAT. W. L. Whittaker and B. L. Baker. (1951) *J. invest. Derm.*, **17**, 69.

Oestrogen applied locally is absorbed and inhibits the growth of hair in a general way: its effect is neutralized by adrenalectomy.

Cortisone ointment completely inhibits the growth of hair on site of application only: adrenalectomy merely serves to accentuate the contrast. J. H. T. D.

STUDIES ON ATABRINE DERMATITIS. I: LONG TERM OBSERVATION OF VETERANS WITH PERMANENT ATROPHIC RESIDUA OF THE DISEASE. I. L. Schamberg. (1951) *J. invest. Derm.*, **17**, 85.

In a certain small proportion of cases of the tropical lichenoid dermatosis symptoms, including pruritus, eczematoid dermatitis and fragility of the skin, have persisted. The author draws a comparison with the condition "familiar to the dermatologist" of persistence or recurrence of inflammatory dermatitis long after contact with the primary aetiologic agent has been severed, and shrewdly observes that the explanation for such chronicity is poorly understood.

J. H. T. D.

PREPARATION OF SKIN POWDER AND SKIN EXTRACTS. A. B. Lerner. (1951) *J. invest. Derm.*, **17**, 251.

To get powdered skin you have first to freeze it into a brittle state and then pass it through a Wiley mill operated in the deep freeze. Even so liquid nitrogen has to be added to prevent thawing at the cutting edges of the blades. This powder becomes a sticky amorphous mass as soon as it thaws.

A pressure of 20 tons to the square inch applied to coarsely chopped skin has failed to squeeze any moisture out of it; but with the little mangle here described you can extract 7 ml. out of 20 g.

J. H. T. D.

EOSINOPHILIC INCLUSION BODIES AND CYTOPLASMIC MASSES IN VERRUCAE. M. J. Strauss, H. Bunting and J. L. Melnick. (1951) *J. invest. Derm.*, **17**, 209.

The inclusion bodies tend to be found in young warts especially of the plantar variety and in young subjects.

J. H. T. D.

STUDIES IN SENSITIZATION TO HALOGENATED HYDROXYQUINOLINES AND RELATED COUPOUNDS. W. Leifer and K. Steiner. (1951) *J. invest. Derm.*, **17**, 233.

Three patients were found to be intolerant of vioform, diodoquin, quinolor and sterosan. Reactions to these and to related substances were investigated by patch testing. The authors concluded that the sensitizing properties reside in the hydroxyl group rather than in the quinoline itself or the halogen radical.

Quinoline is represented as a double benzene ring with a nitrogen atom in position 1 ; pyridine is the same thing with a single benzene ring. The addition of a carboxyl group in various positions of this ring yields acids, one of which is nicotinic acid. The subjects of this study also gave positive patch tests to these acids but not to pyridine itself. J. H. T. D.

SHIFTING OF CATIONS IN THE CEREBROSPINAL FLUID AS A CAUSE OF PRURITUS. H. Königstein. (1951) *J. invest. Derm.*, **17**, 99.

This important paper is almost unreadable through jargon, inept translation and lack of editorial care. If the practical scientist and research worker believes that his task ends with the completion of his experiments and the recording of his results then he should associate himself with a colleague who can read and write. One of the references to the literature (in the author's own tongue) contains 7 spelling mistakes.

Salts of potassium caesium and ammonium administered intracisternally produce paroxysms of scratching in rabbits and cats. So do bromides ; hence the popularity of potassium bromide among physicians—not necessarily homoeopathic—who probably quite correctly attribute the symptom to "nerves." Strontium too showed a "strong prurigenous effect," and strontium bromide 20 years ago was the principal ingredient of a fashionable intravenous injection for eczema. Fortunately you have to give a good big dose of anything intravenously for it to reach the C.S.F., as the author discovered when he tried to raise the C.S.F. calcium by 20%. The required dose in fact kills the animal unless it is injected very slowly. In the case of man a 10% solution of calcium chloride would have to be given at a rate of 10 c.c. per lb. of body weight to do any good. Calcium, in addition to its general sedative action on the C.N.S., has a specific effect in the C.S.F. in neutralizing the effects not only of added potassium salts, sodium bromide, ammonium chloride, etc., but also of substances like pilocarpine and morphine. This action is in turn neutralized by oxalates and alkaline phosphates, which of course precipitate the calcium.

Parathyroid plus vitamin D, though it raised the C.S.F. calcium only a very little, appeared to be effective with cats in raising (the author writes *lowering*) the threshold to prurigenous influences.

The reviewer regrets that his terms of reference do not permit him completely to rewrite this interesting paper : but he hopes that perhaps he will have encouraged to read it some of those who might have been repelled by its literary austerities. J. H. T. D.

PRANTAL IN THE TREATMENT OF HYPERHIDROSIS. L. M. Nelson. (1951) *J. invest. Derm.*, **17**, 207.

If Prantal, a quaternary amine (N, N-dimethyl-4-pyridylidene-1, 1-diphenylmethane methyl sulphate), is really so superior to Banthine that it diminishes perspiration without at the same time causing dryness of the mouth, dilatation of the eyes and a decreased force of the urinary stream, then it is obvious that we are on a good thing. J. H. T. D.

ALLERGIC REACTIVITY TO SIMPLE ALIPHATIC ACIDS IN MAN. A. J. Weil and H. E. Rogers. (1951) *J. invest. Derm.*, **17**, 227.

This is thought to be the first case recorded in the literature of sensitivity to acetic acid in man, though analogous reaction in experimental animals has already been reported by one of the authors.

A woman laboratory worker, with a family history of allergy and a personal history of intolerance of formaldehyde, developed a rash which corresponded in area to contact with objects contaminated with acetic acid. Patch tests produced a strong immediate reaction as well as a very slight and fugitive eczematoid one. Reactivity to intradermal injection, at all events moderate, disappeared after a period of abstention from contact, but returned as soon as the dermatitis was allowed to recur by renewed exposure. Sensitivity was limited to the acid and its anhydride. Salts and polysaccharides containing acetyl groups gave negative reactions. There appeared to be no increased vulnerability of the skin to acids in general.

J. H. T. D.

CLINICAL EXPERIENCES WITH RUTIN IN THE THERAPY OF DERMATITIS TOXICA. H. J. Sonneck. (1952) *Derm. Wschr.*, 125, 31.

The author treated a series of patients with rutin (rutabion): 66 had dermatitis medicamentosa and 8 primula dermatitis. Widespread weeping types responded better than the circumscribed. Doses of 300–500 mg. *t.i.d.* by mouth or parentally were necessary and all other treatment was stopped. The rutin was found to have a diuretic action and to diminish oedema and itching; in some patients redness and scaling persisted despite continued rutin treatment. Patch tests with the drugs, peroral tests and in a few instances the Prausnitz-Küstner test seemed to indicate that rutin diminished the sensitivity reaction: this increased again on stopping rutin. He suggests that rutin exerts its effect by increasing capillary resistance, reducing oedema and preventing the deposition of allergens in the skin. In spite of the known antagonism between sulphonamides and rutin he feels it would be wise to give rutin where sulphonamide therapy must be prolonged, but sufficiently large doses would be necessary. Of the series 39% cleared up on rutin, 39% were improved, and the remainder were not benefited. The author feels that the treatment time is shortened in most patients with the use of rutin. M. S. S.

INDUSTRIAL SKIN INJURY BY CONTACT INSECTICIDE E605. W. Schneider. (1952) *Derm. Wschr.*, 125, 321.

E605 (folidol) is an alkalized phosphorus compound widely used in Germany like the earlier DDT, and is an even more effective insecticide. It is very dangerous to man when not used in the correct dilution or according to instructions, hence its undesirable popularity as a suicidal agent. The author discusses its toxicology, and notes as remarkable the weakness or paralysis of muscles in severe poisoning.

The author gives the clinical findings and history in 2 patients of his own who developed dermatitis following the use of E605. Patch tests were negative, but in one patient spraying the flexure of one arm with the usual 2% emulsion gave rise to a recrudescence of the dermatitis. Gardeners seem particularly prone to sensitization, especially when using the spray. Preventive measures should be directed particularly against inhalation, and contact with the eyes and conjunctivae. M. S. S.

IS THROMBOPHLEBITIS MIGRANS A SISTER DISEASE OF ENDANGITIS OBLITERANS OF WINIWARTER-BUERGER? B. Lüdner and H. S. F. Scheffler. (1942) *Derm. Wschr.*, 125, 341.

In the opinion of the authors the two diseases in the title are related. A non-specific inflammatory reaction of the vasa vasorum of arteries or veins may lead to endangitis obliterans or thrombophlebitis migrans. The authors review the literature, and base their conclusions on two patients investigated histologically. With the capillary microscope they found no evidence of a generalized capillaritis. Photographs and photomicrographs accompany the text. M. S. S.

WATER ECONOMY UNDER VIGANTOL. L. K. Eckes. (1952) *Derm. Wschr.*, 125, 348.

The author applied Volhard's test to 25 patients under treatment with Vigantol, giving 800 c.c. of water and 3 units of hyphophysin. In 15 controls not on Vigantol there was diminished urinary excretion during the first four hours. In patients on up to 100 mg. of Vigantol a paradoxical effect was obtained –66% more fluid was excreted in the four hours than in the controls, showing absence of a hypophysin effect. This was even more marked (over 100% increase) when doses greater than 100 mg. were given, more fluid being excreted than had been administered: the author does not regard this paradoxical effect as evidence of intolerance. He points out that this influence on excretion is undoubtedly an extrarenal one probably of hormonal nature, perhaps a diencephalon-hyphophysis effect. M. S. S.

INVESTIGATIONS ON FILTRABLE FORMS OF MYCOBACTERIUM TUBERCULOSIS IN LUPUS VULGARIS. J. Meyer-Rohn. (1952) *Derm. Wschr.*, 125, 439.

The author reviews the literature on the subject, and gives his findings following cultural microscopic and animal investigations with three strains of tubercle bacilli. He describes his technique in detail. A bovine strain led to generalized tuberculosis on animal inoculation, but this was found to be due to a faulty Berkefeld filter and the finding was discounted. The experiments yielded no evidence of an ultravirus form of the tubercle bacillus even with the electron microscope. Tubercle bacilli cultures from two lupus vulgaris patients yielded a similar result. M. S. S.

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